Diastolic Function – Theory and Assessment

February 23, 2007

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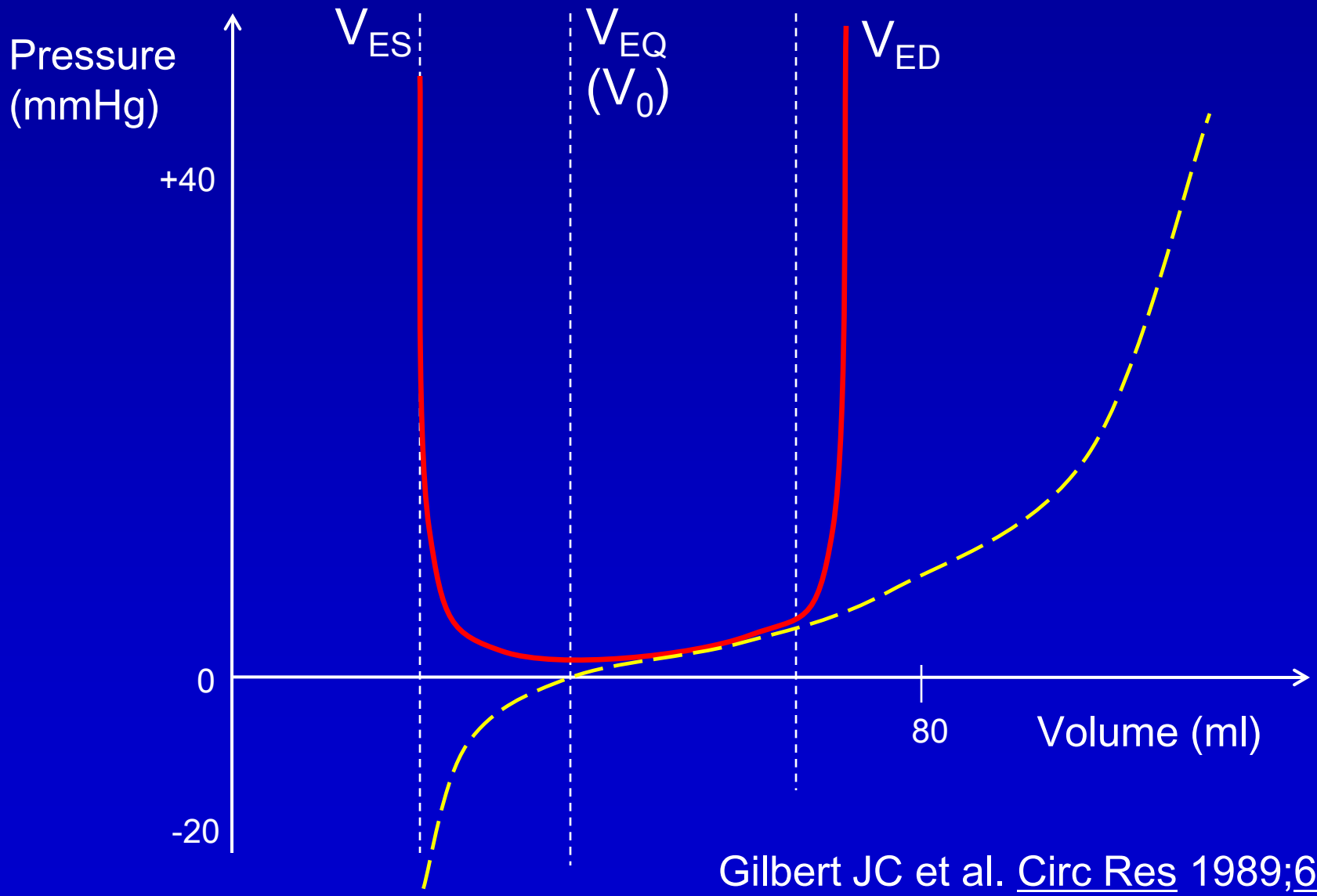
Diastole - Summary

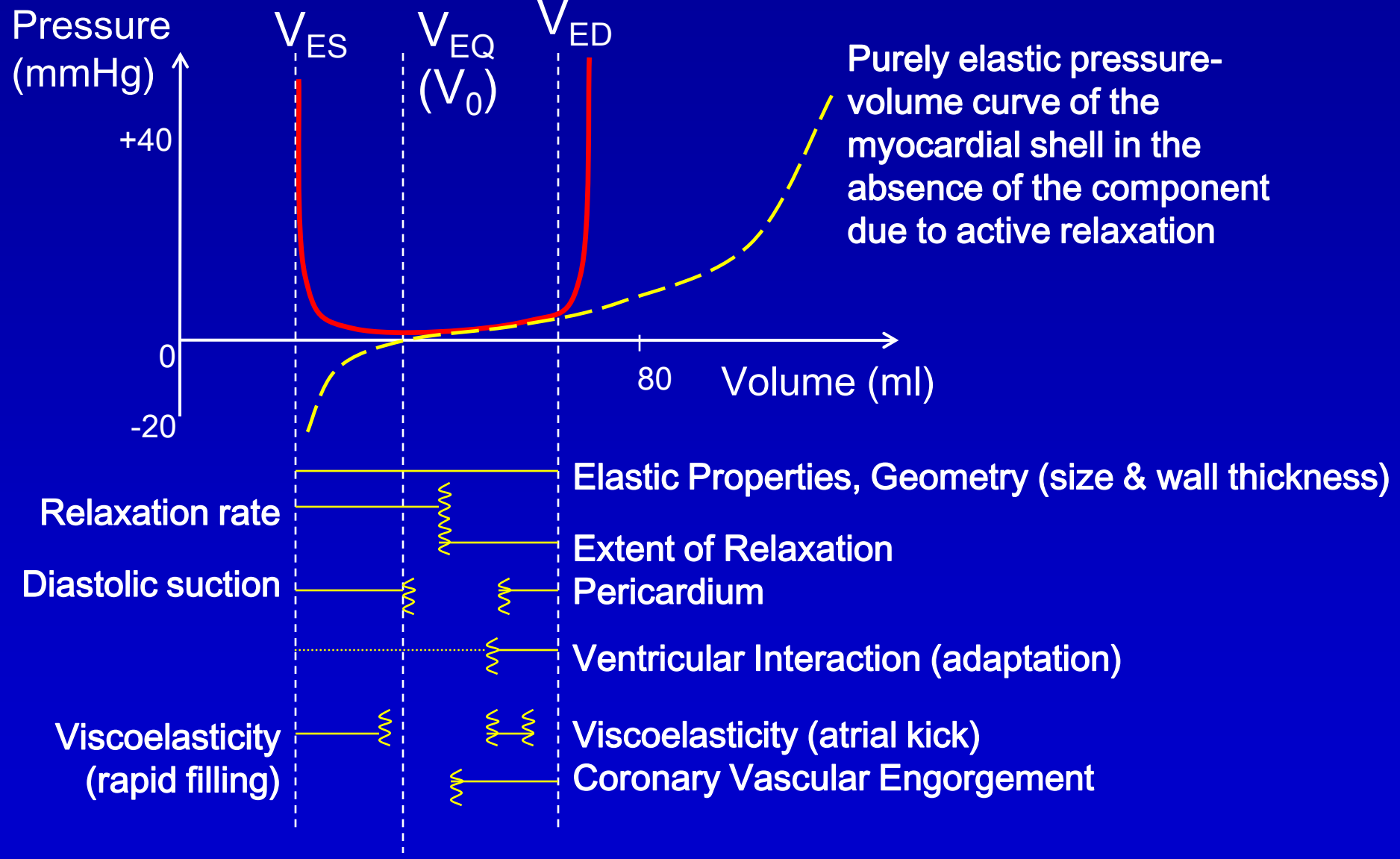
- Relaxation
  - Active process
  - Measurable during isovolumic relaxation
  - Heart rate effects
- Passive ventricular properties
  - Geometry: wall thickness and radius
  - Histology: cellular composition, collagen
  - Extrinsic factors
- (Atrial systole – atrial transport – stepchild)

Diastolic function - Suction

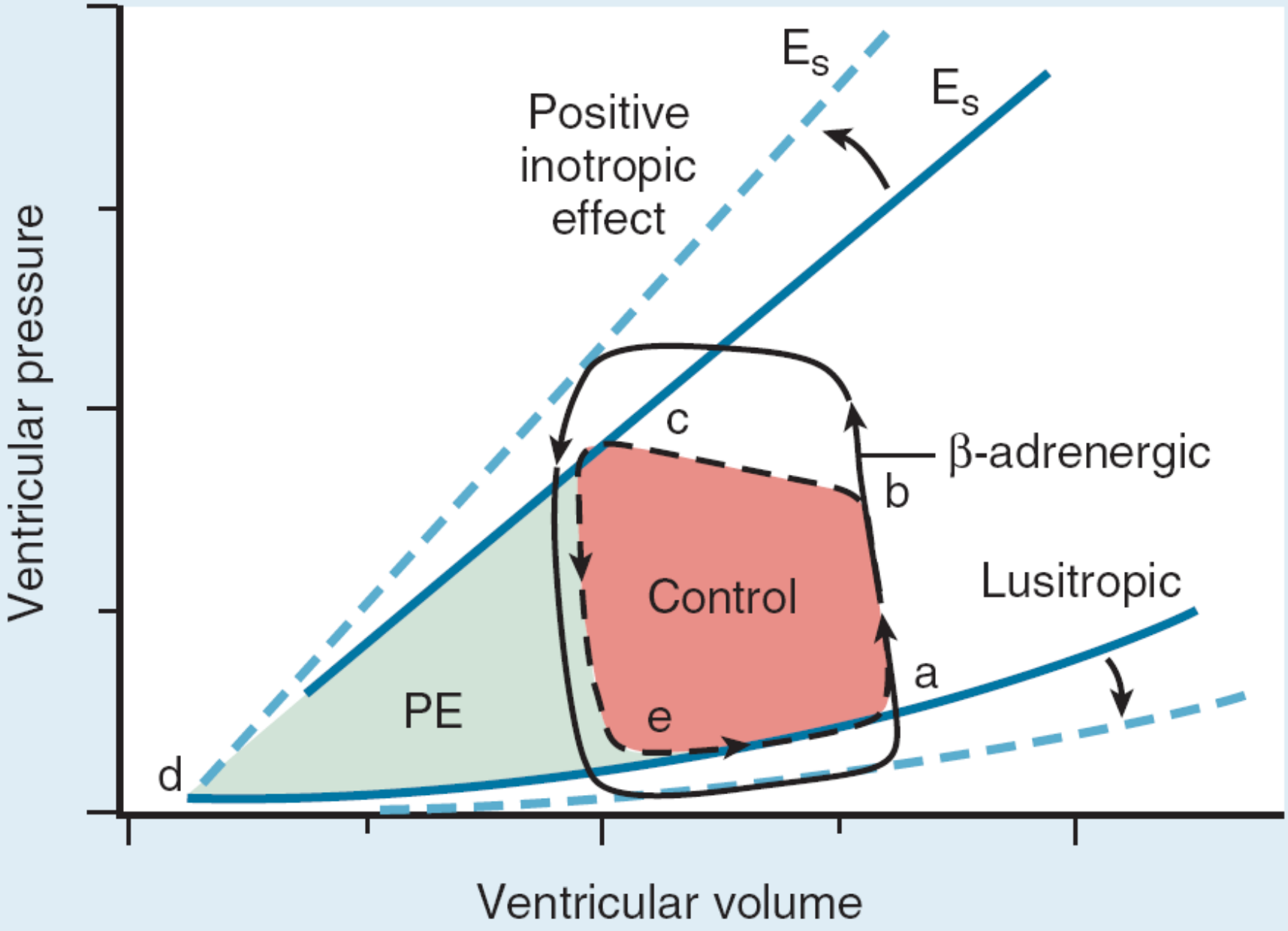


Gilbert JC et al. Circ Res 1989;64:828.

Diastolic function (Suction)



Adapted from Gilbert JC et al. Circ Res 1989;64:828.



Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.

Physiology of Diastole

- Diastole: traditionally, from S2 to S1
  - More specifically, onset is at maximal elastance, slightly before aortic valve closure (protodiastole)

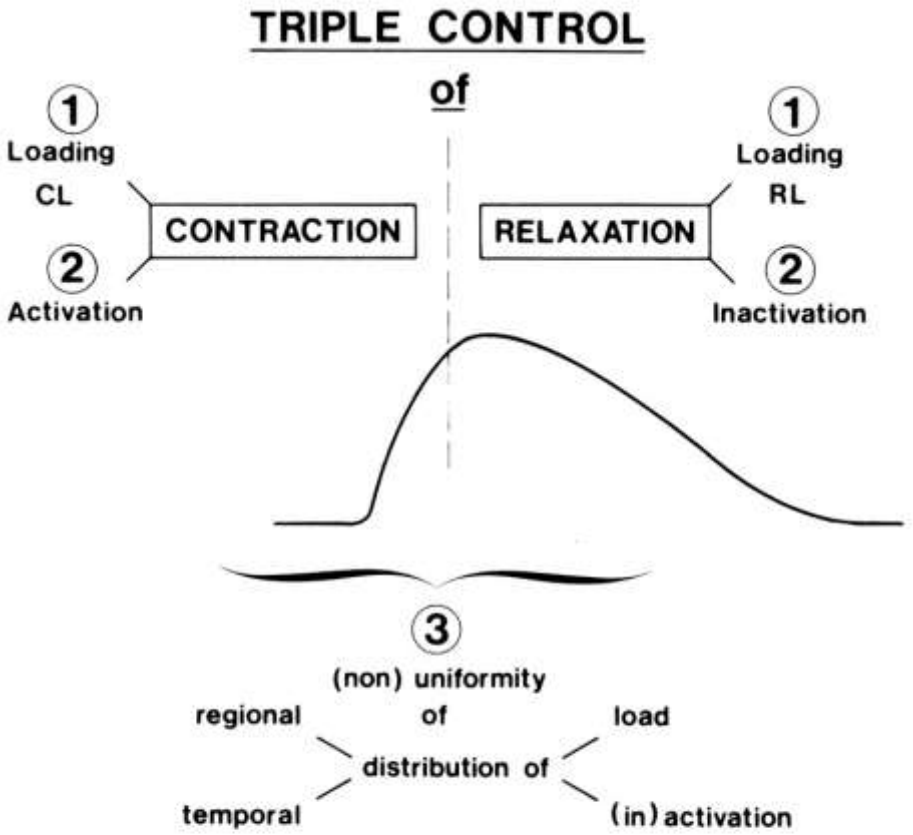


Fig 1. Triple control of the contraction and relaxation phases of the cardiac cycle. The curve in the middle of the figure gives the time course of an isometric contraction of isolated cardiac muscle (see Fig 3) and is used as a reference to illustrate the time course of an entire cardiac cycle.

Physiology of Diastole

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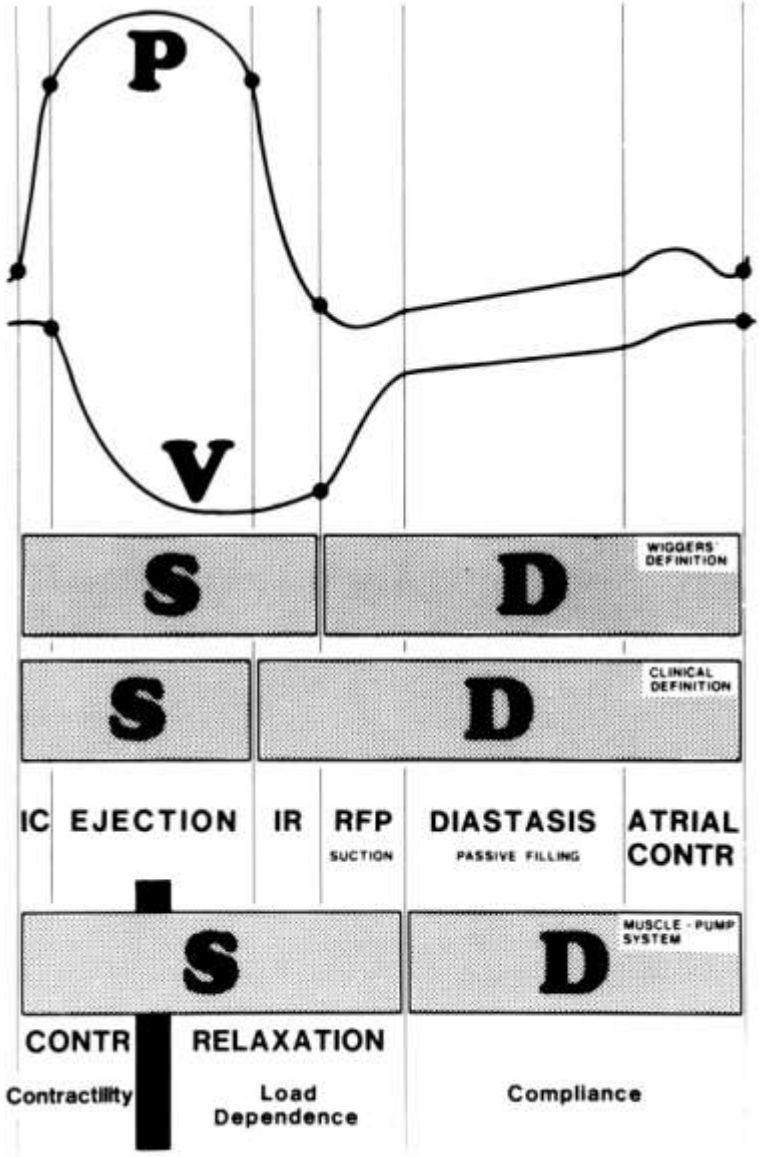


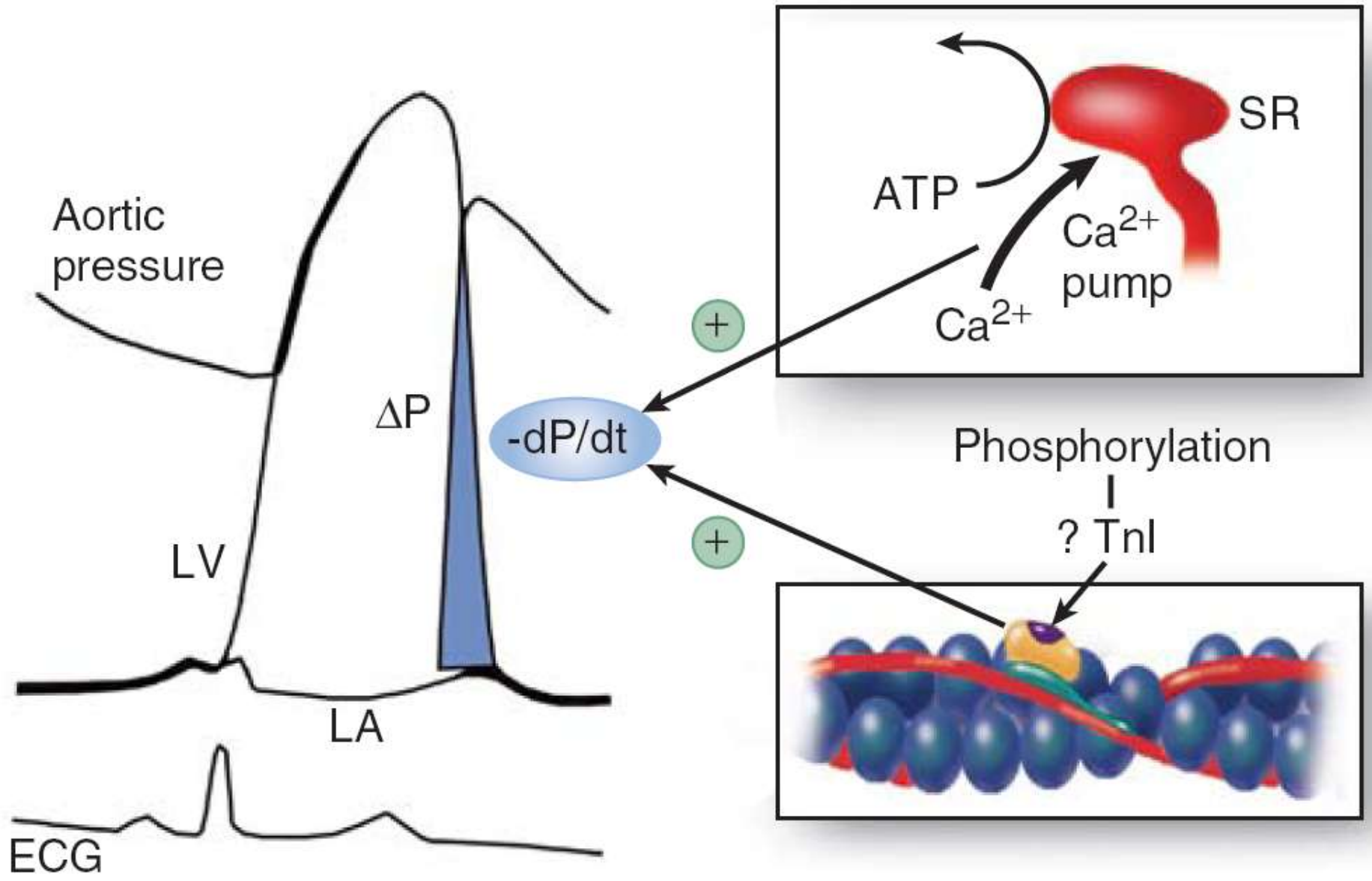
Fig 2. Subdivision of the cardiac cycle into systole and diastole. P and V, pressure and volume curves as a function of time; S, systole; D, diastole; IC, isovolumic contraction; IR, isovolumic relaxation; RFP, rapid filling phase; contr, contraction.

Physiology of Diastole

- Diastole: traditionally, from S2 to S1
  - More specifically, onset is at maximal elastance, slightly before aortic valve closure (protodiastole)
- Normal function: LV accepts adequate filling volume to maintain cardiac output at normal operating pressure
- Active diastole: Lusitropic function
- Passive diastole: mechanical properties

Relaxation Factors

- Cytosolic Ca++ must fall
- Viscoelastic properties of myocardium
- Phosphorylation of troponin I accelerates relaxation
- Systolic load accelerates relaxation



Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.

Relaxation Factors – (1)

- Cytosolic Ca++ must fall – (1)
  - 10-fold, from 100 nM to 10 nM*
  - Requires ATP used by SERCA2a (sarcoendoplasmic reticulum Ca2+-adenosine triphosphatase), the dominant cardiac isoform using 1 ATP for 2 Ca++ ions
  - SERCA2a constitutes ~90% of SR protein

*Petrashevskaya NN et al. J Mol Cell Cardiol. 2002;34:885.
Braunwald's Heart Disease, 7th Ed. Opie LH. Ch 19, p. 464, 481.

Relaxation Factors – (2)

- Cytosolic Ca++ must fall – (2)
  - SERCA2a is regulated by phosphorylation of phospholamban for reuptake of Ca++ into SR (dephosphorylated phospholamban is inhibitory**)
  - Phospholamban is phosphorylated at at least 2 sites
    - Ser-10 by PKC** (in vitro only)
    - Ser-16 β-adrenergic stimulation to cAMP to PKA**
    - Thr-17 Calcium ions and calmodulin-dependent protein kinase**

**Zhao W et al. J Mol Cell Cardiol. 2004;37:607
Braunwald's Heart Disease, 7th Ed. Opie LH. Ch 19, p. 464, 481.

Relaxation Factors – (3)

- Viscoelastic properties of myocardium
- Phosphorylation of troponin I accelerates relaxation
- Systolic load accelerates relaxation

**Zhao W et al. J Mol Cell Cardiol. 2004;37:607
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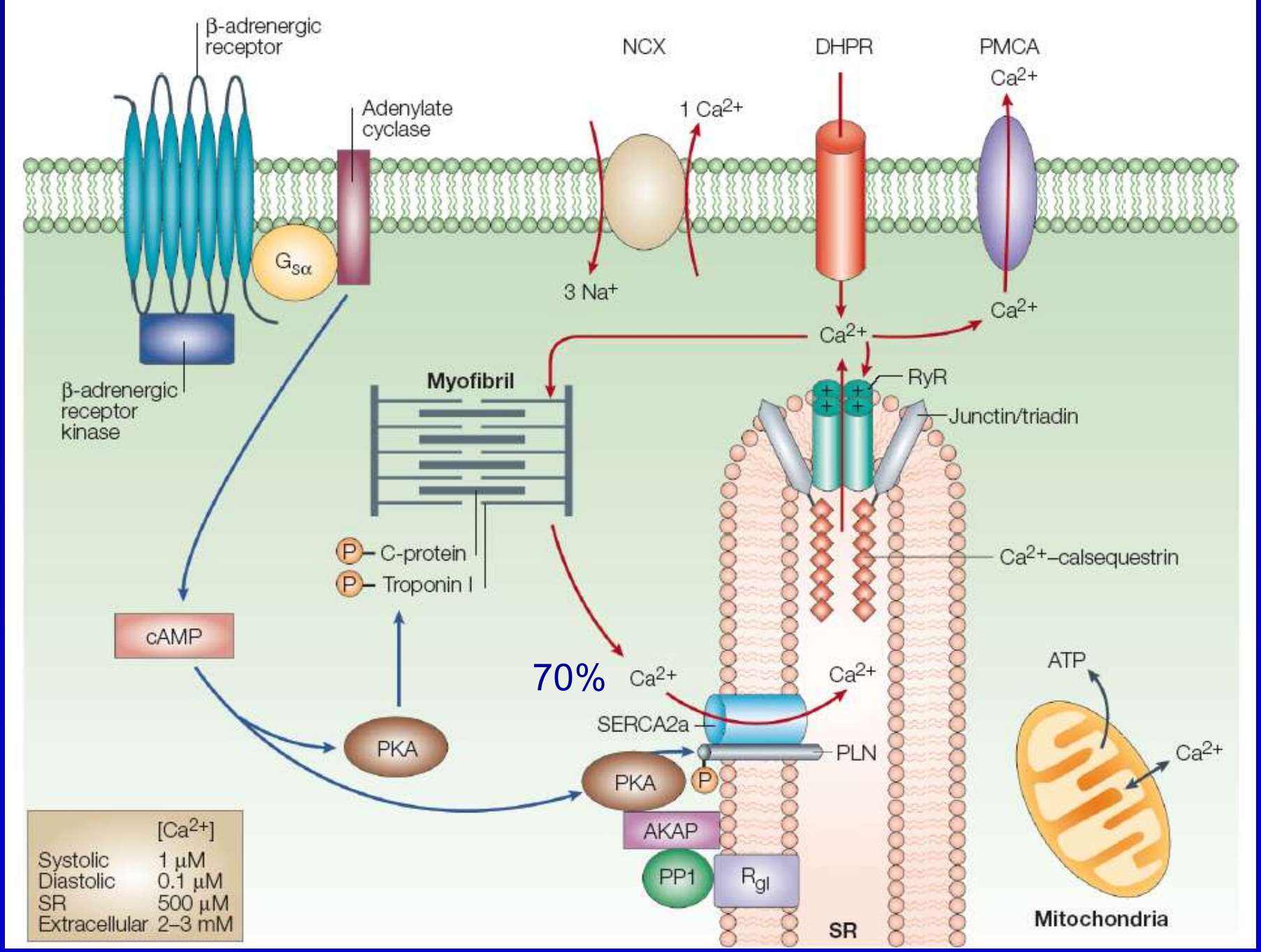
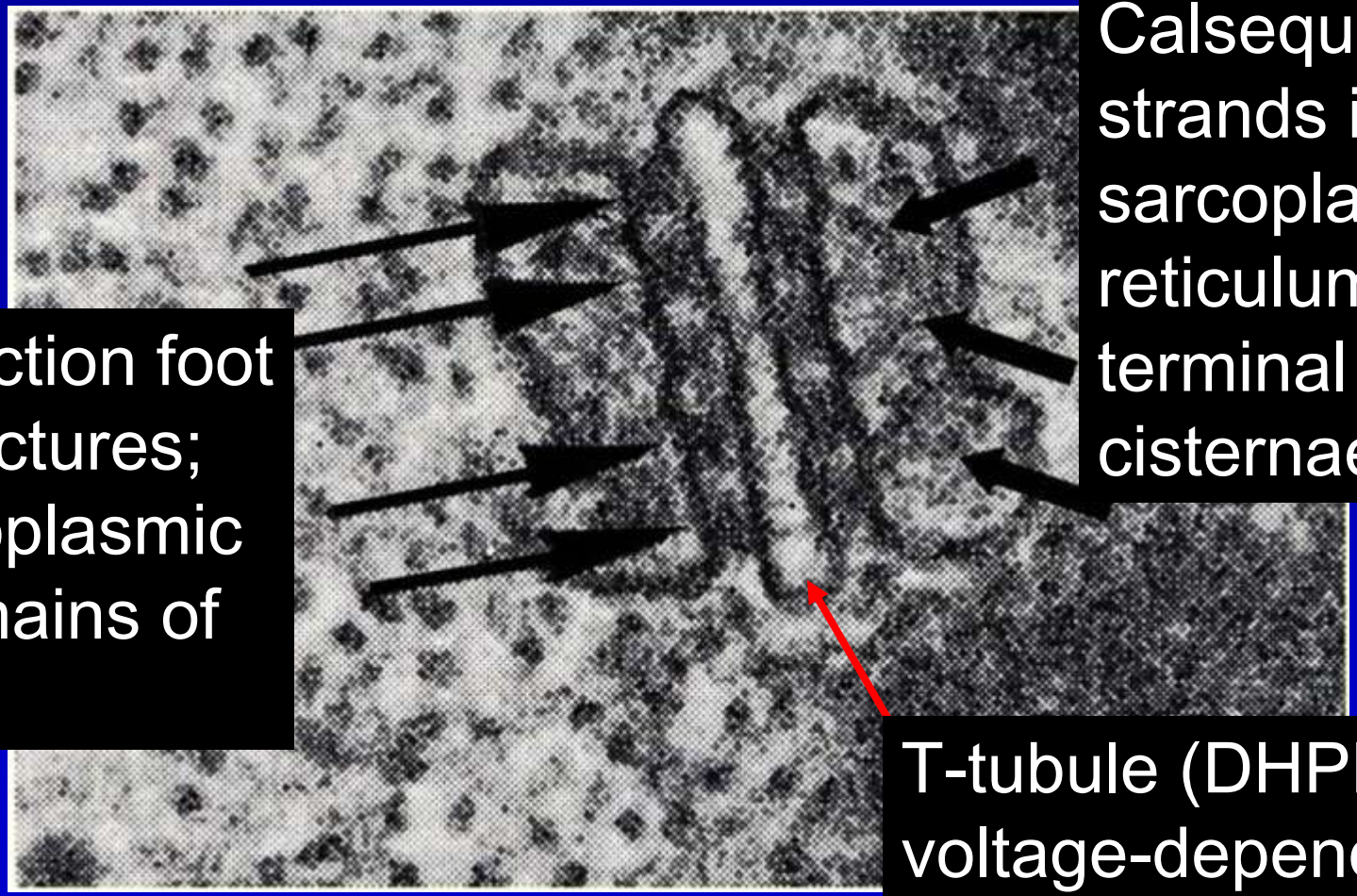


MacLennan DH et al. Nature Medicine 2003;4:566

Triad Junction of T-tubule and Sarcoplasmic Reticulum



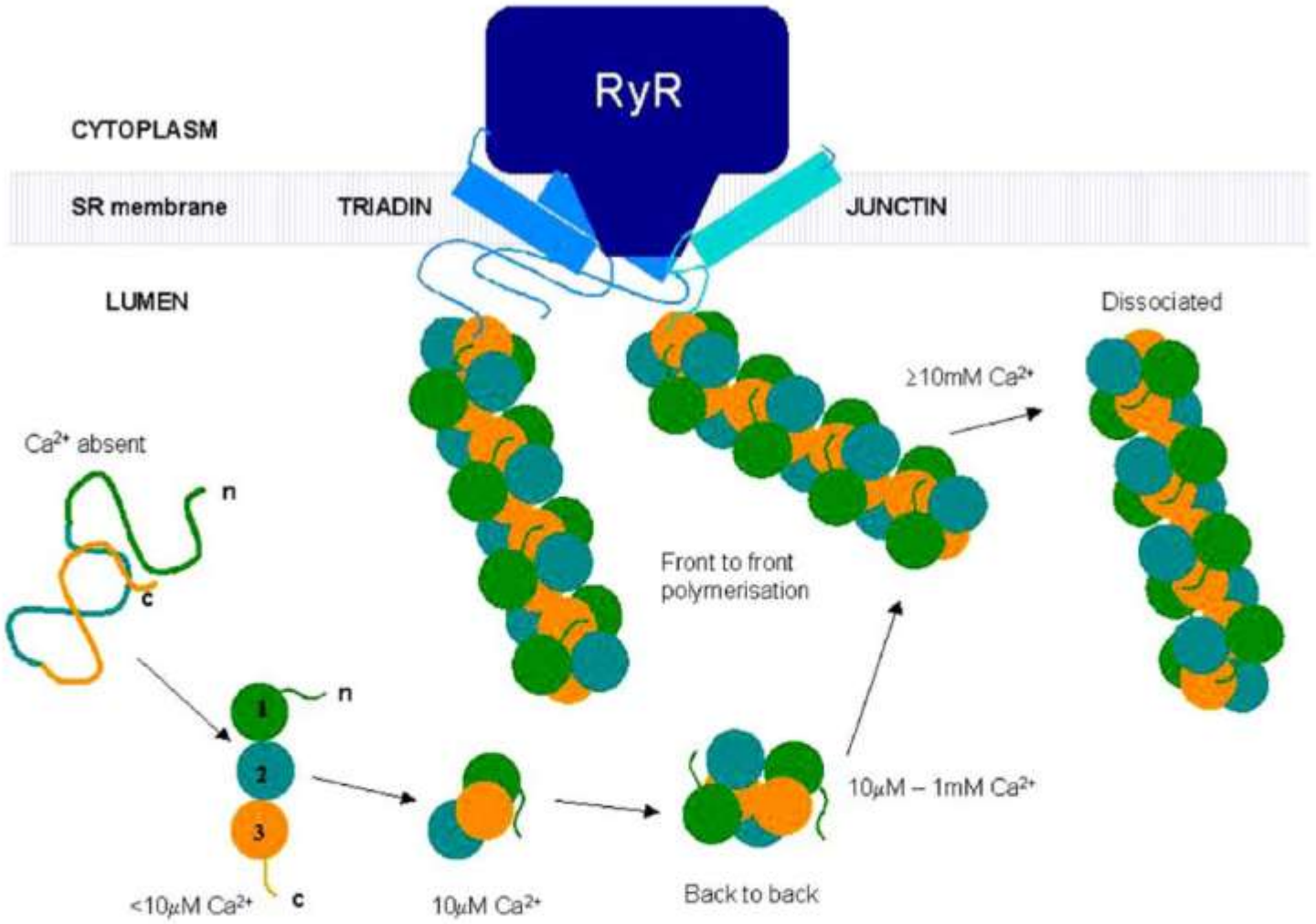
Calsequestrin strands in sarcoplasmic reticulum terminal cisternae

Junction foot structures; cytoplasmic domains of Ryr

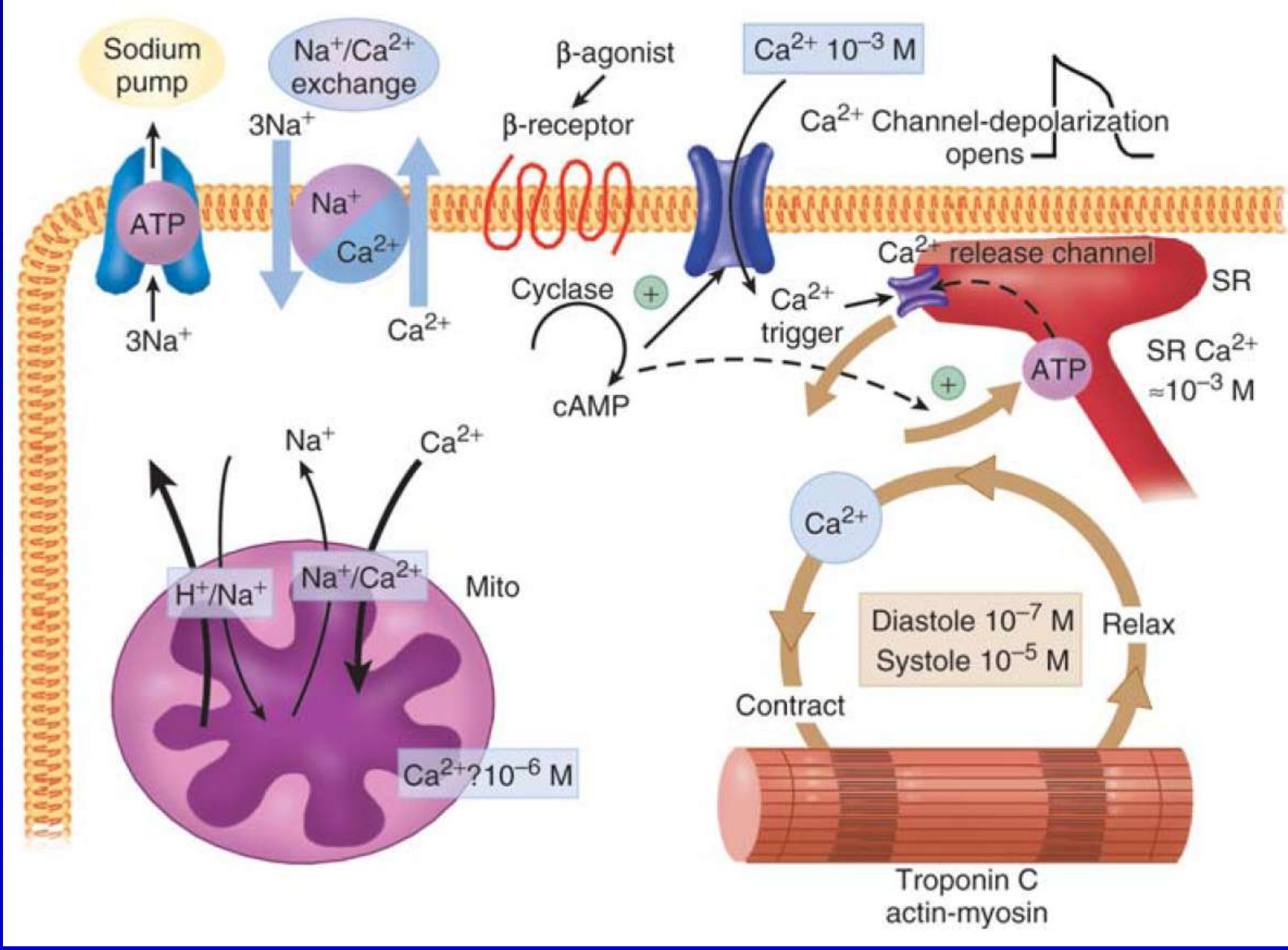
T-tubule (DHPR, voltage-dependent Large Ca^{++} channel)

Beard NA et al. Prog Biophys Mol Biol. 2004;85:33.

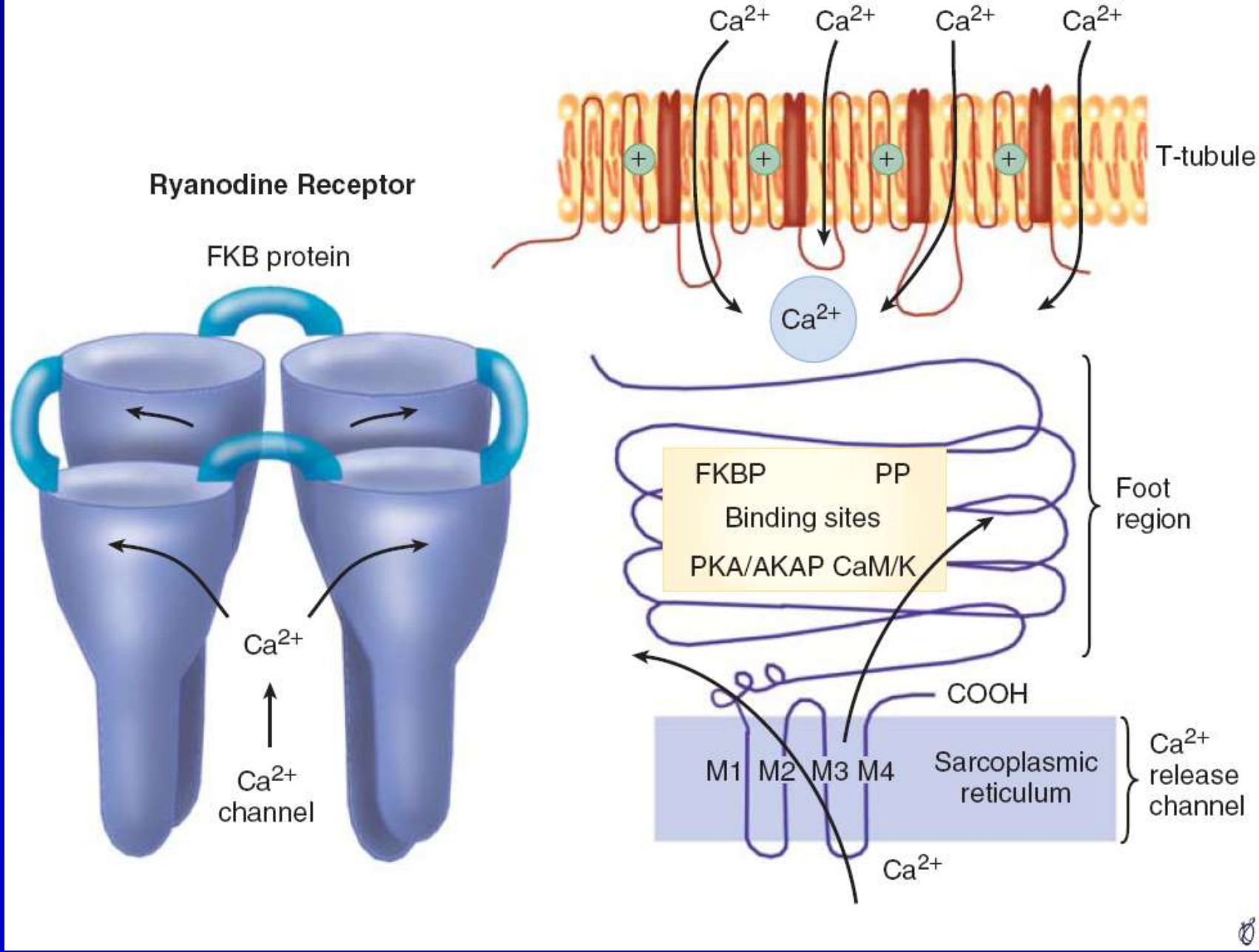
Calsequestrin and the RyR



Beard NA et al. Prog Biophys Mol Biol. 2004;85:33.



Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.



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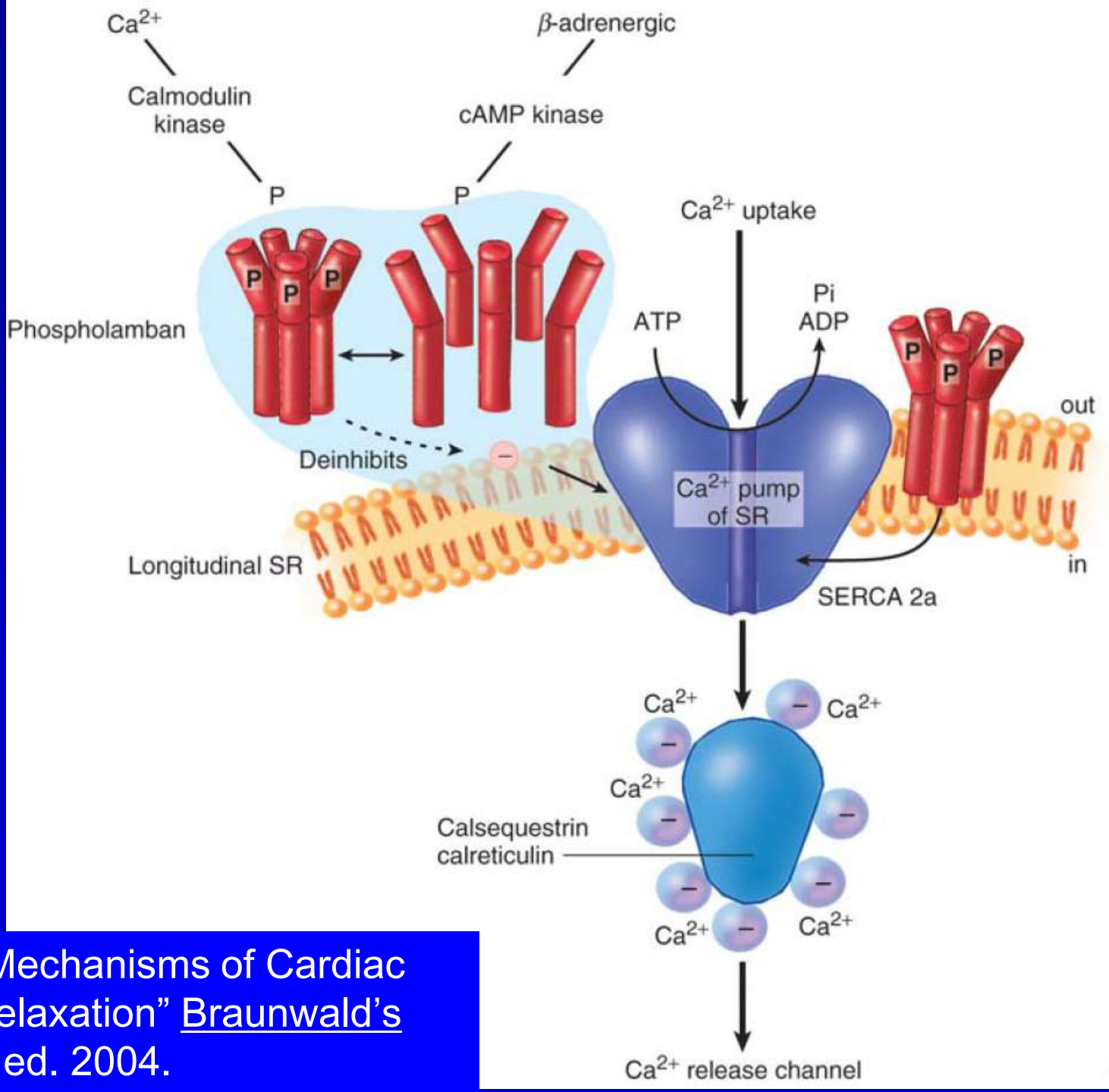
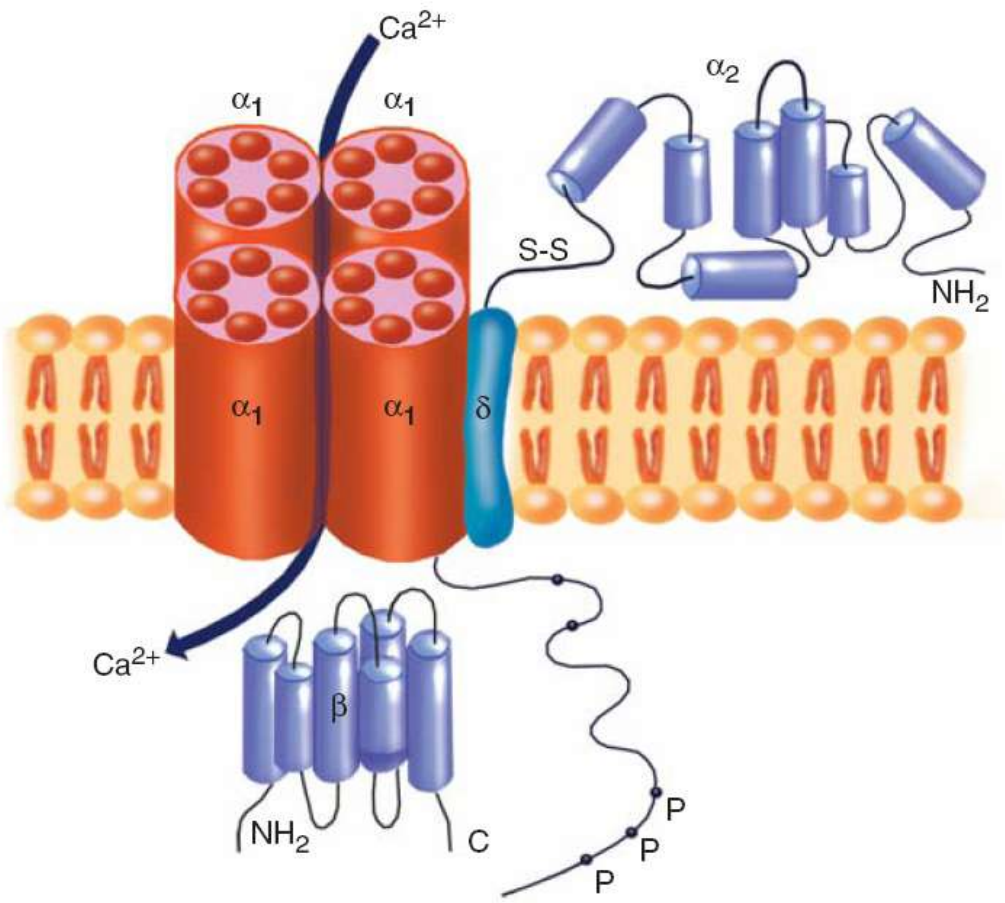
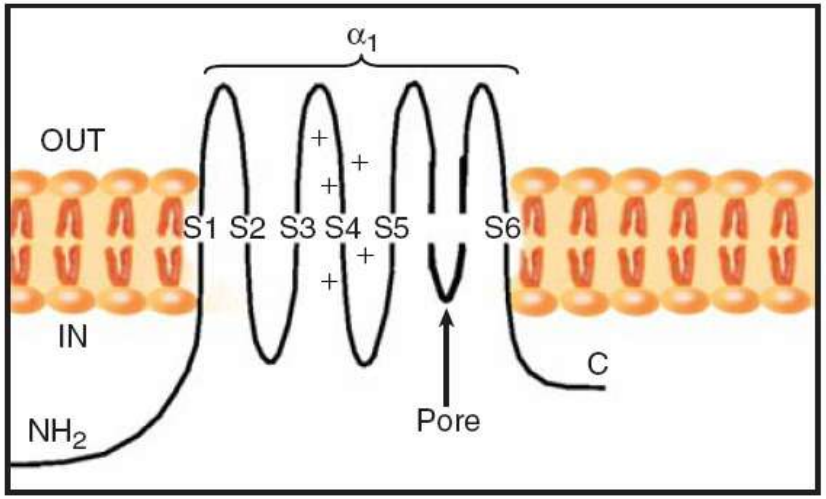
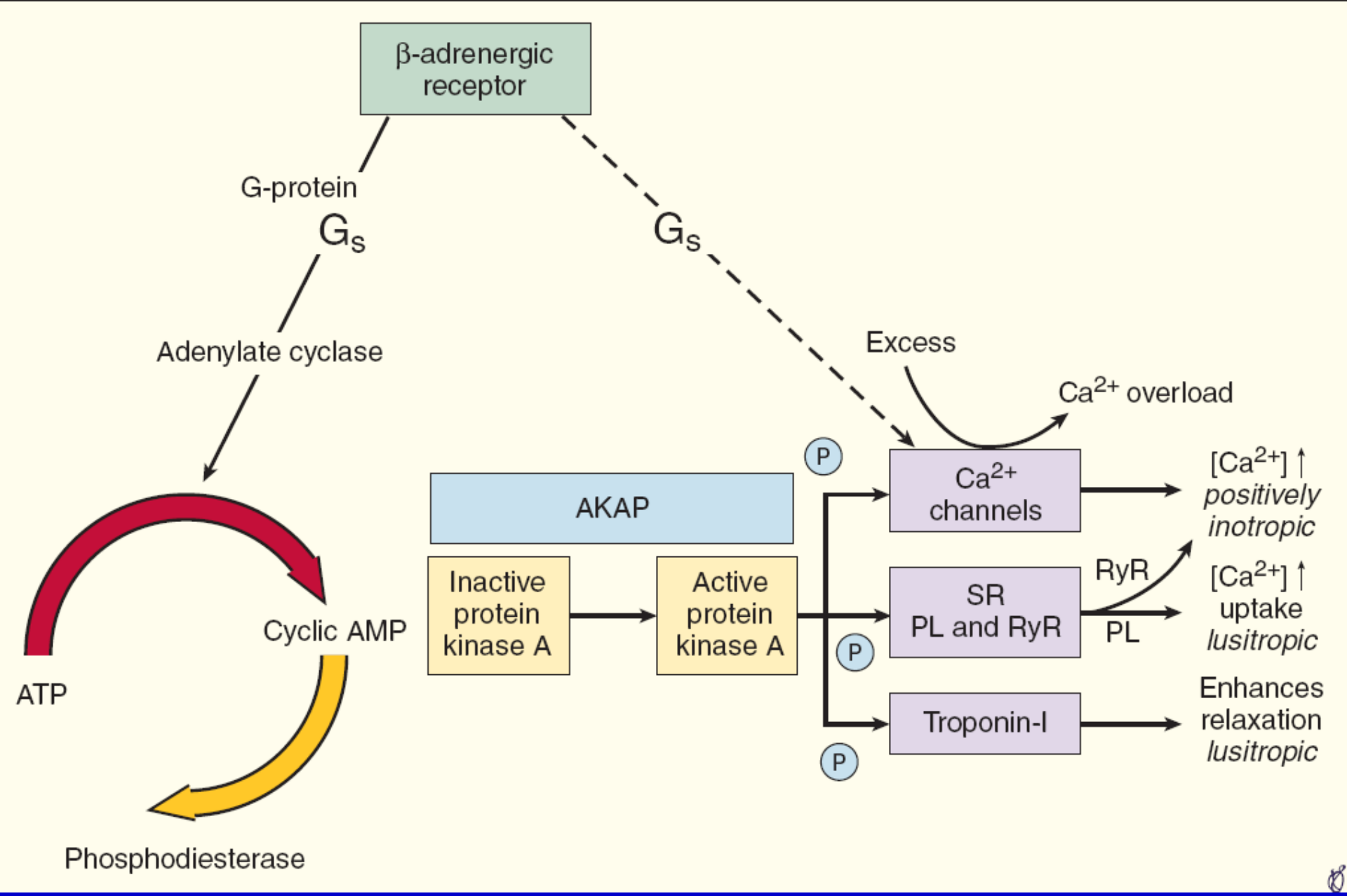


Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.

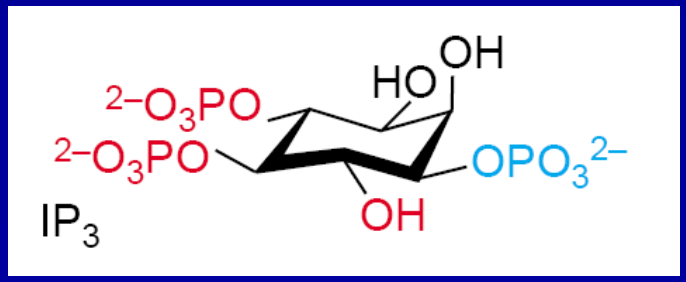




Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.

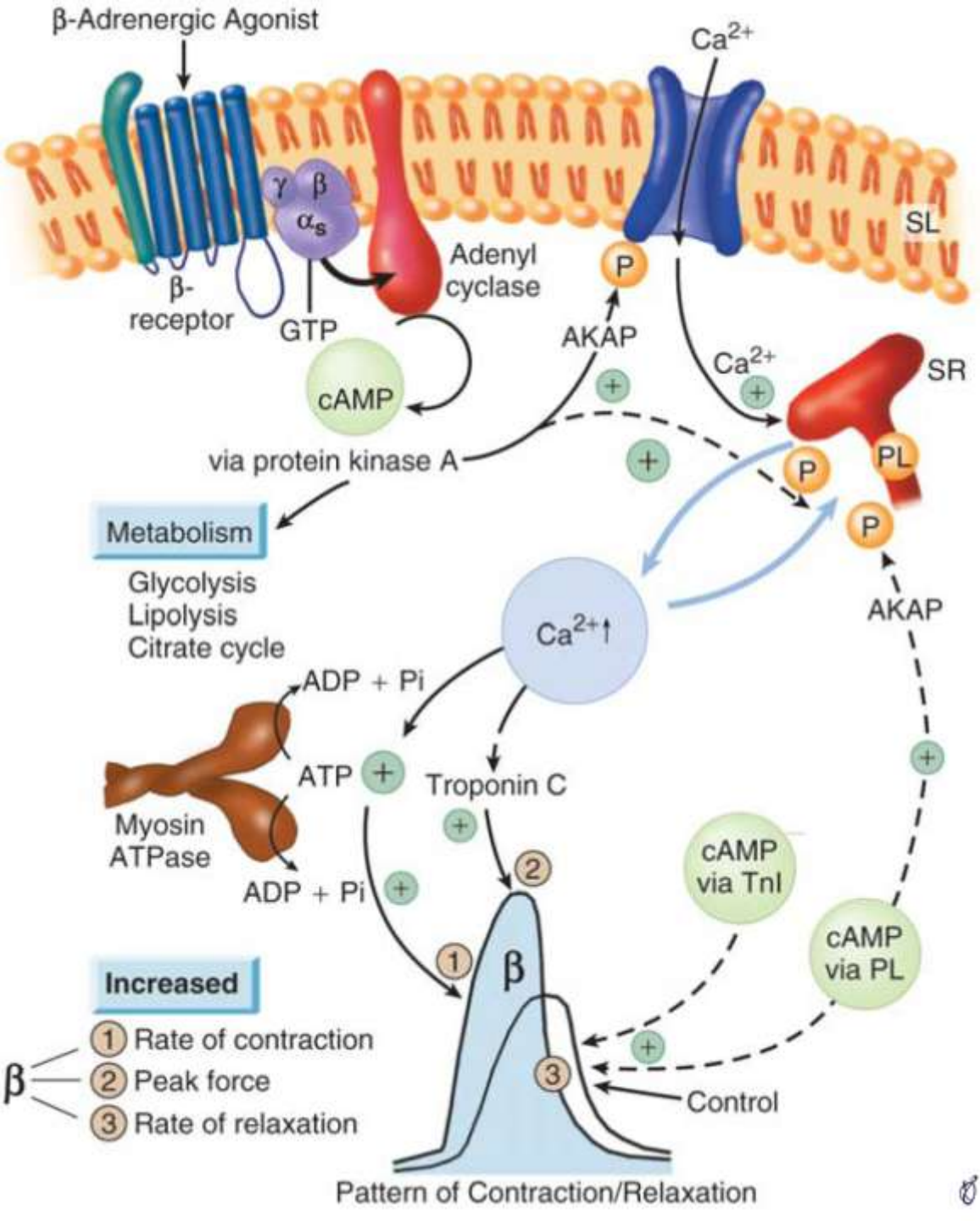


Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.



Taylor CW. da Fonseca PC. Morris EP. IP(3) receptors: the search for structure. [Review] [70 refs] [Journal Article. Review. Review, Tutorial] *Trends in Biochemical Sciences. 29(4):210-9, 2004 Apr*

Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.



Active diastole: Lusitropic function

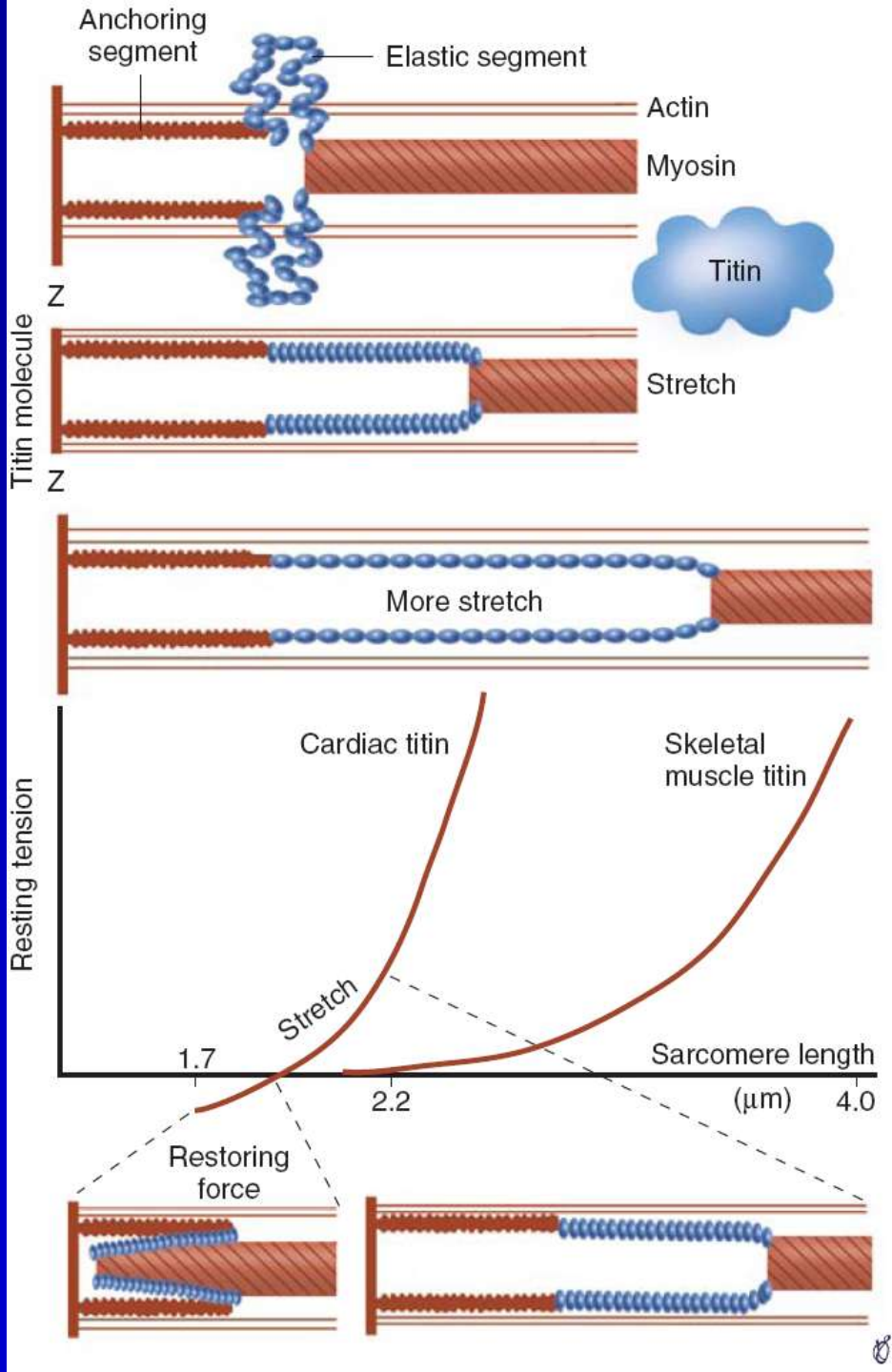
- Myocyte relaxation
  - kinetics of crossbridge cycling (slower cycling slows relaxation, such as high afterload in early systole)
  - affinity of Ca++ for TnC (higher affinity slows relaxation)
  - activity of Ca++ reuptake and extrusion (lower activity of SERCA2 or Na-Ca exchanger slows relaxation, such as ischemia)

Active diastole: Lusitropic function

- Restorative forces (titin compression ? Probably not)
  - End-systolic LV volume < equilibrium LV volume
  - Leads to suction
  - Negative pressure reached rarely in MS, otherwise not seen due to LV filling, also damped by viscous forces
  - Pressures below 0 seen in the cath lab are not real, but are due to underdamped waveforms

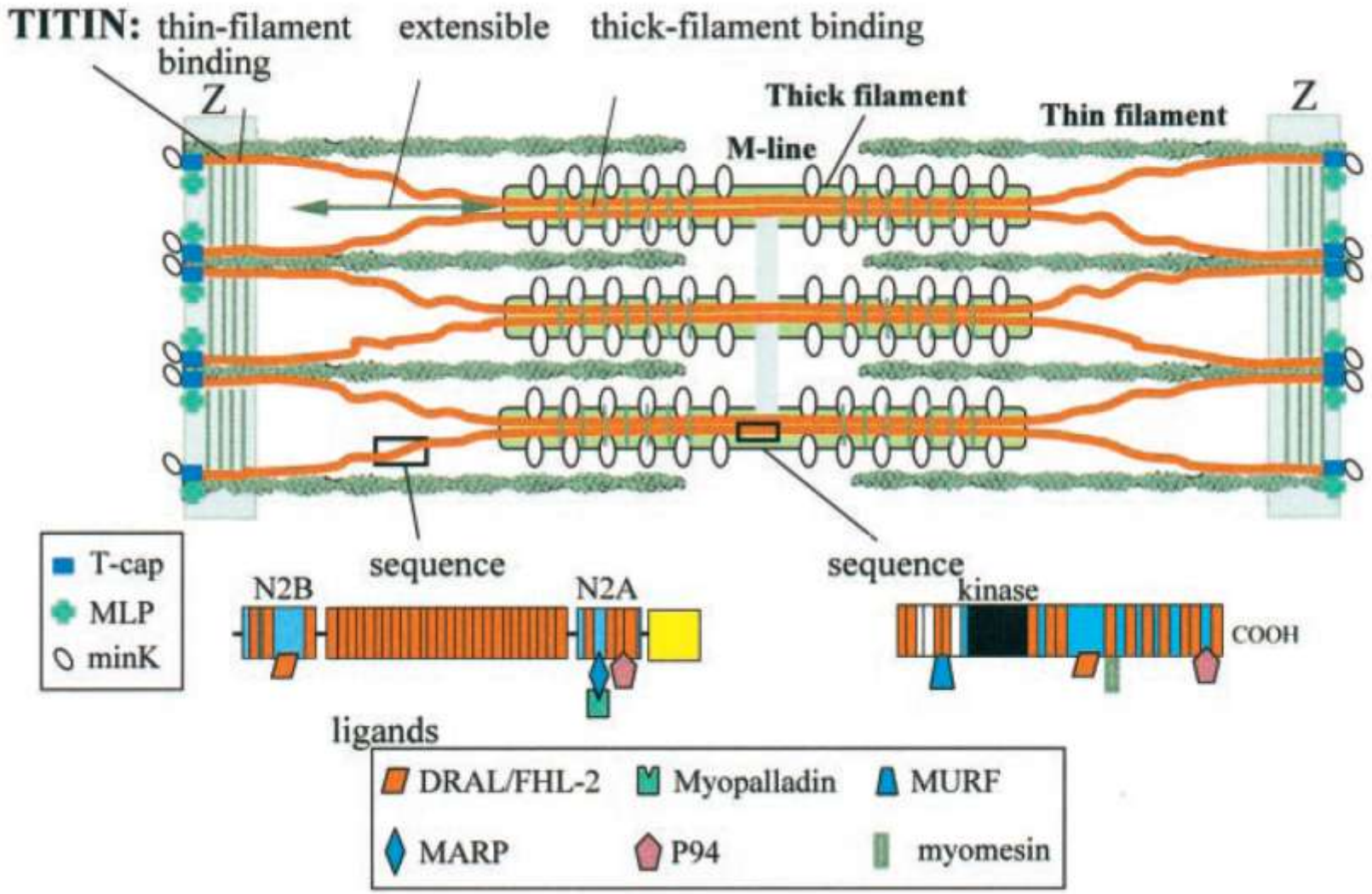
Passive (Fully Relaxed) Diastole

- Compliance = Δvolume/Δpressure, (ΔV/ΔP)
- End-diastolic pressure-volume relation (EDPVR)
- Factors:
  - Ratio of volume to wall thickness
  - Intrinsic stiffness of myocardial tissue
    - At low volumes largely due to properties of titin
    - At high volumes largely due to properties of connective tissue
  - Stiffness is change in stress (force/cross sectional area) related to change in strain (change from initial length or area)
- External constraints: parietal pericardium, myocardial vascular blood volume (turgor), atrial function



Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.

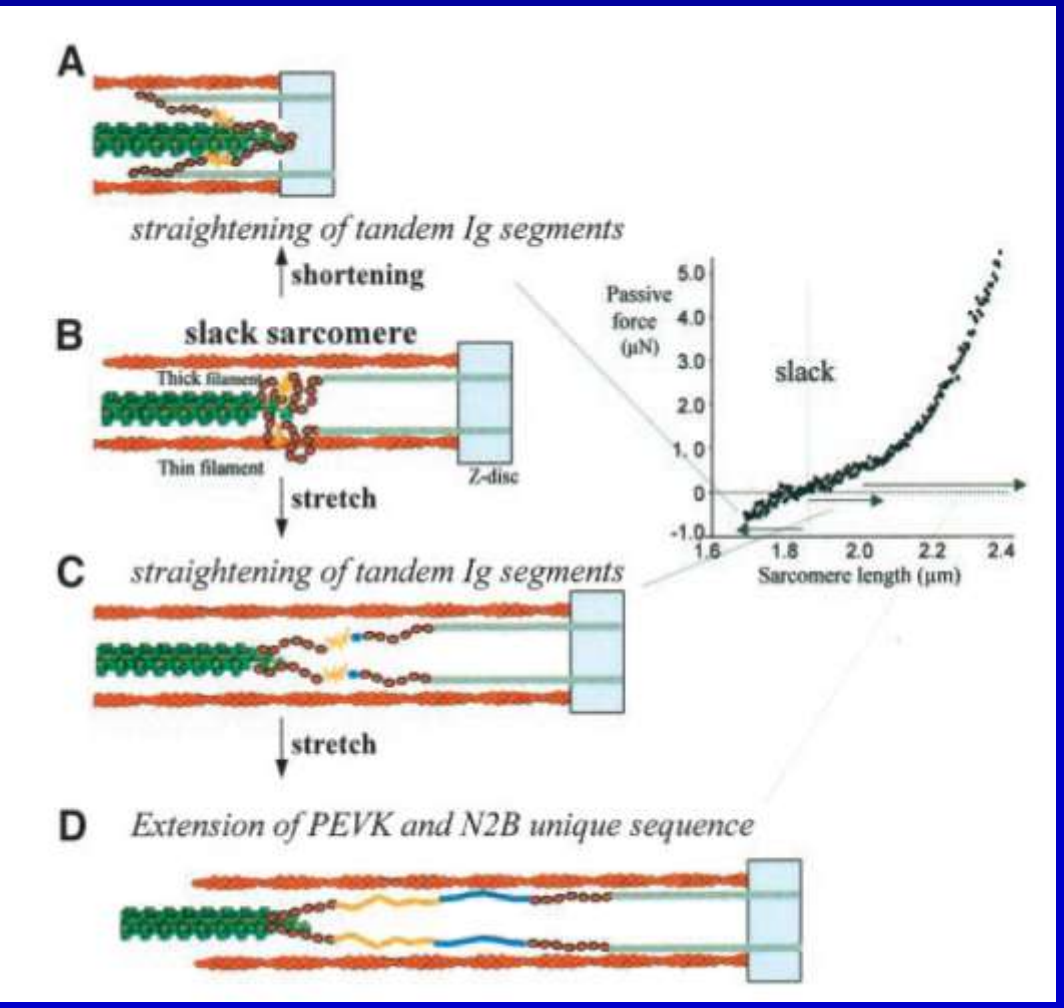
Titin in Diastolic Function



Titin's behavior itself is viscoelastic

Granzier HL et al. Circ Res 2004;94:284

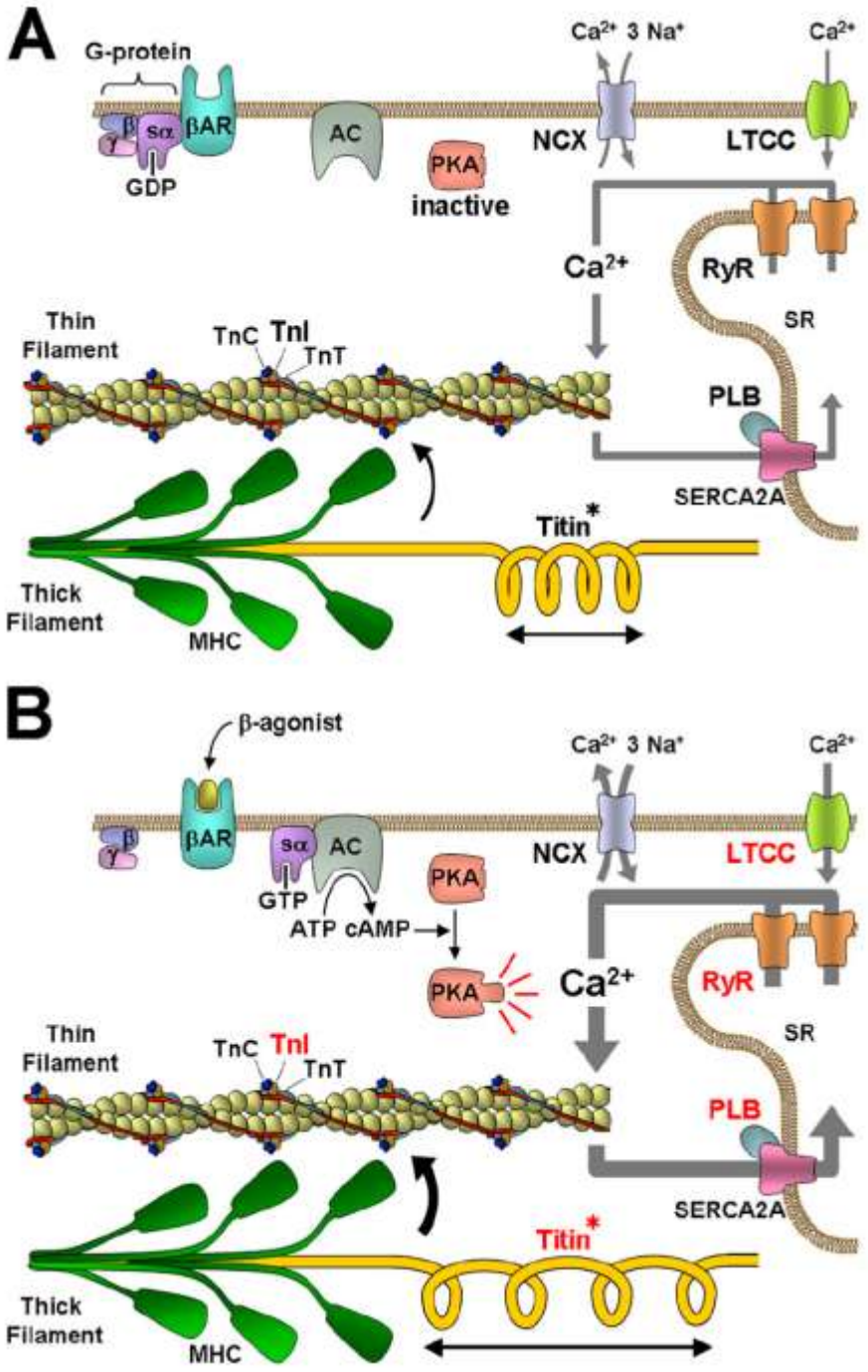
Titin in Diastolic Function



Mechanism of passive and restoring force generation. Titin's extensible region is in a shortened state in slack sarcomeres (B) and extends on sarcomere stretch (C and D), lowering conformational entropy and giving rise to an entropic force, known as passive force. When slack sarcomeres shorten to below the slack length (A), the thick filament moves into titin's incompressible near Z-disc region (in gray) and the extensible region now extends in a direction opposite of that during stretch, developing restoring force. Figure not to scale.

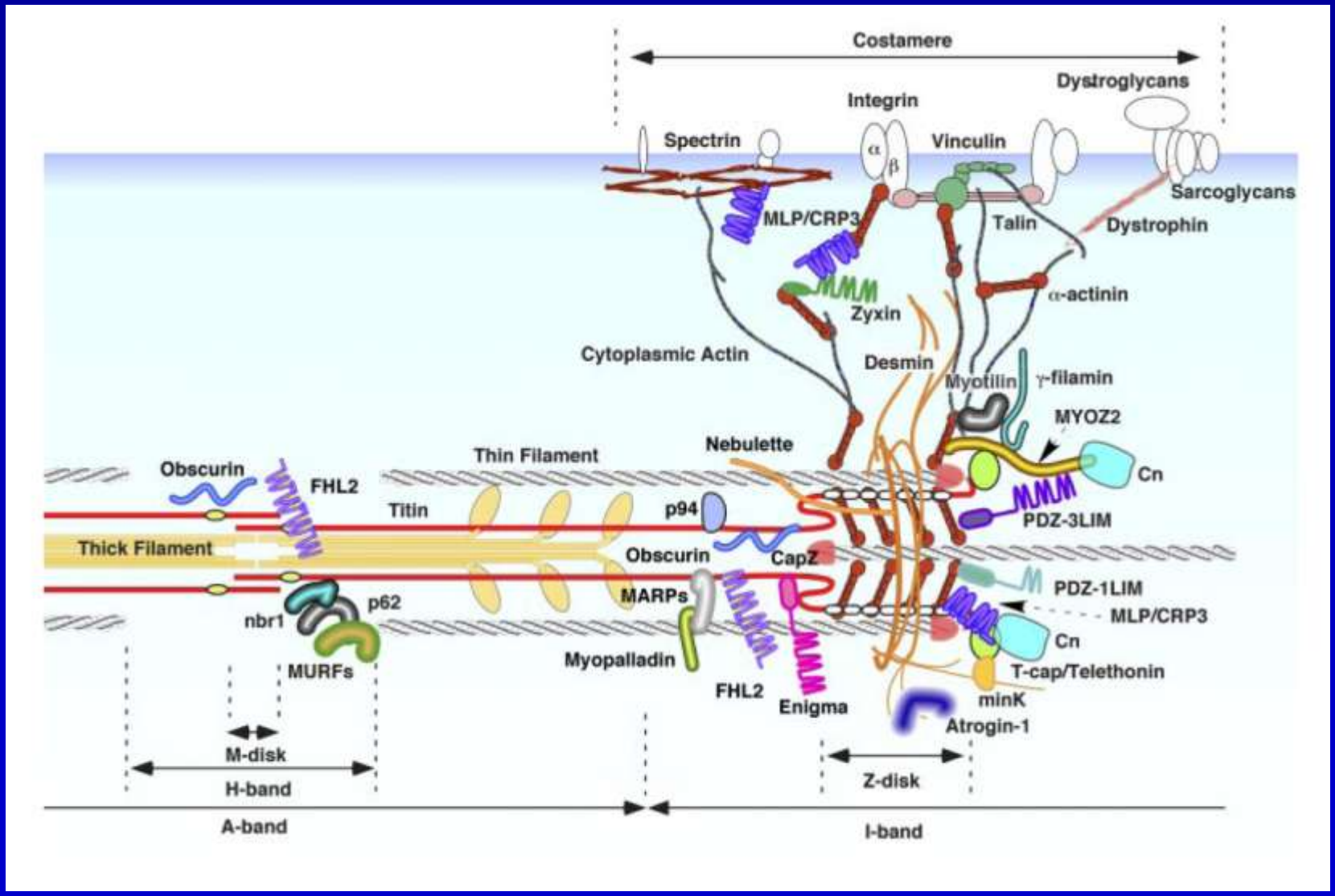
Granzier HL et al. Circ Res 2004;94:284

Titin in Diastolic Function



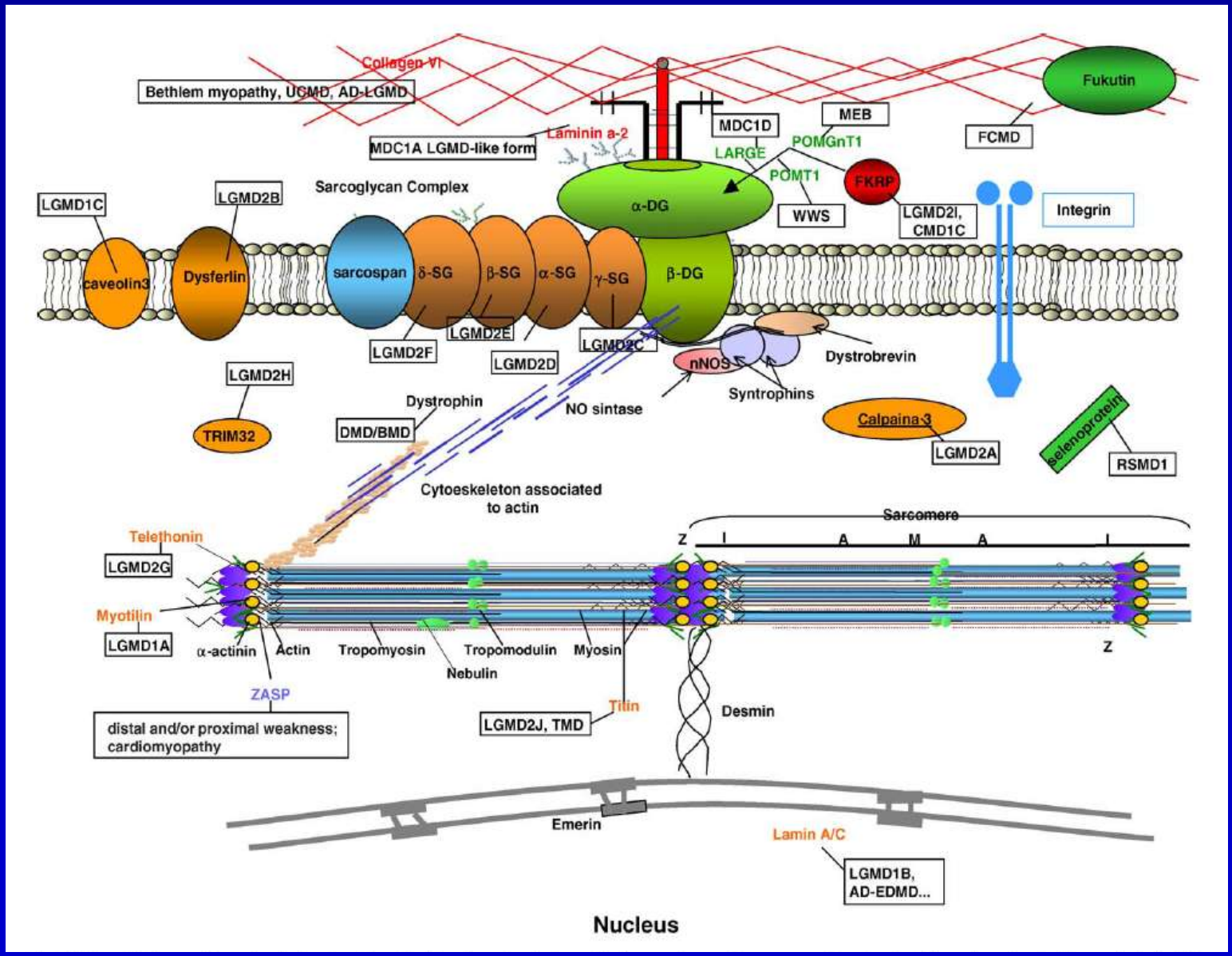
Lim CC et al. J Gen Physiol. 2005;125:249.

The Z-Disk of the Sarcomere



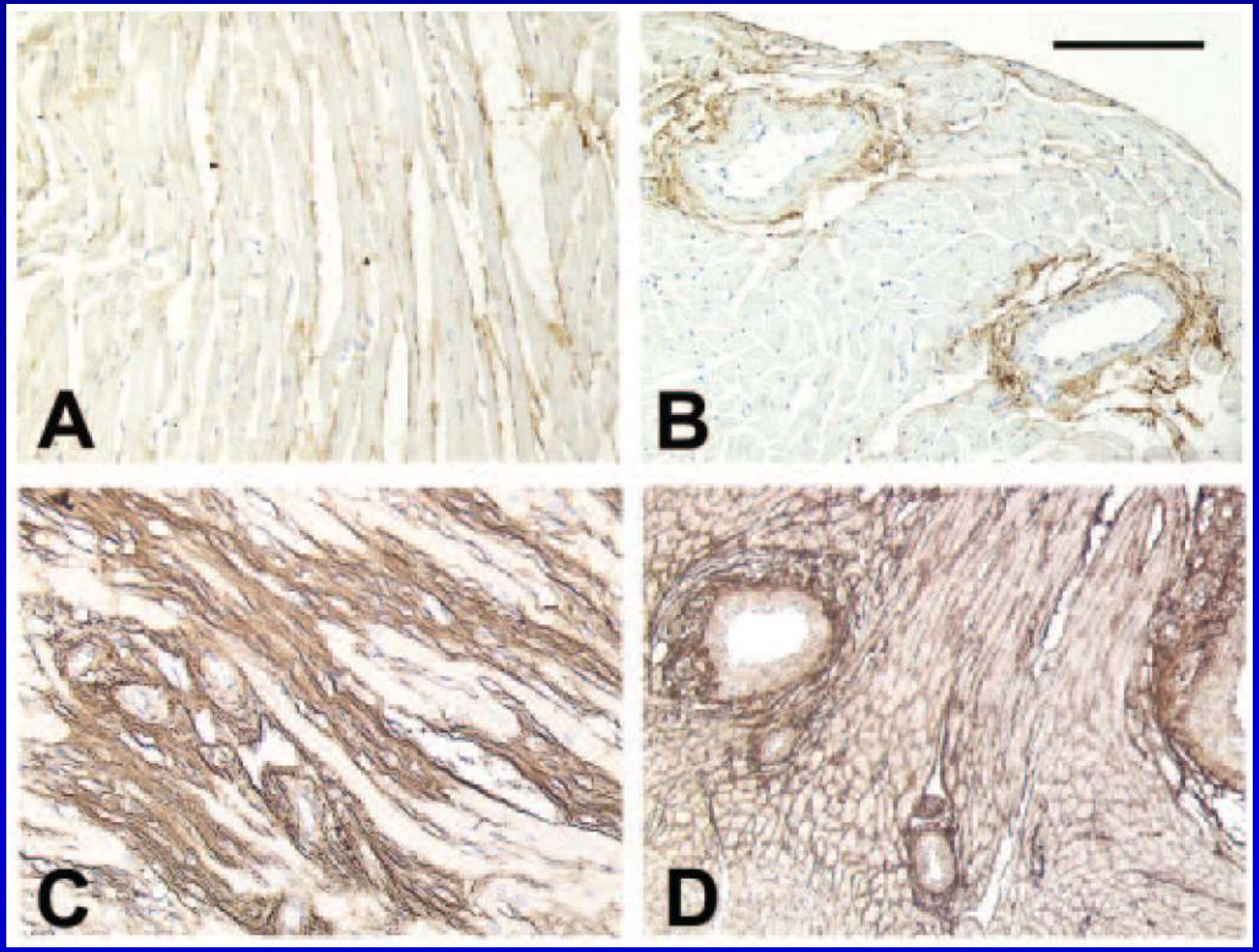
Hoshijima, M. AJP-Heart Circ Physiol • 2006;290:1313

Spectrum of Dystrophic Syndromes

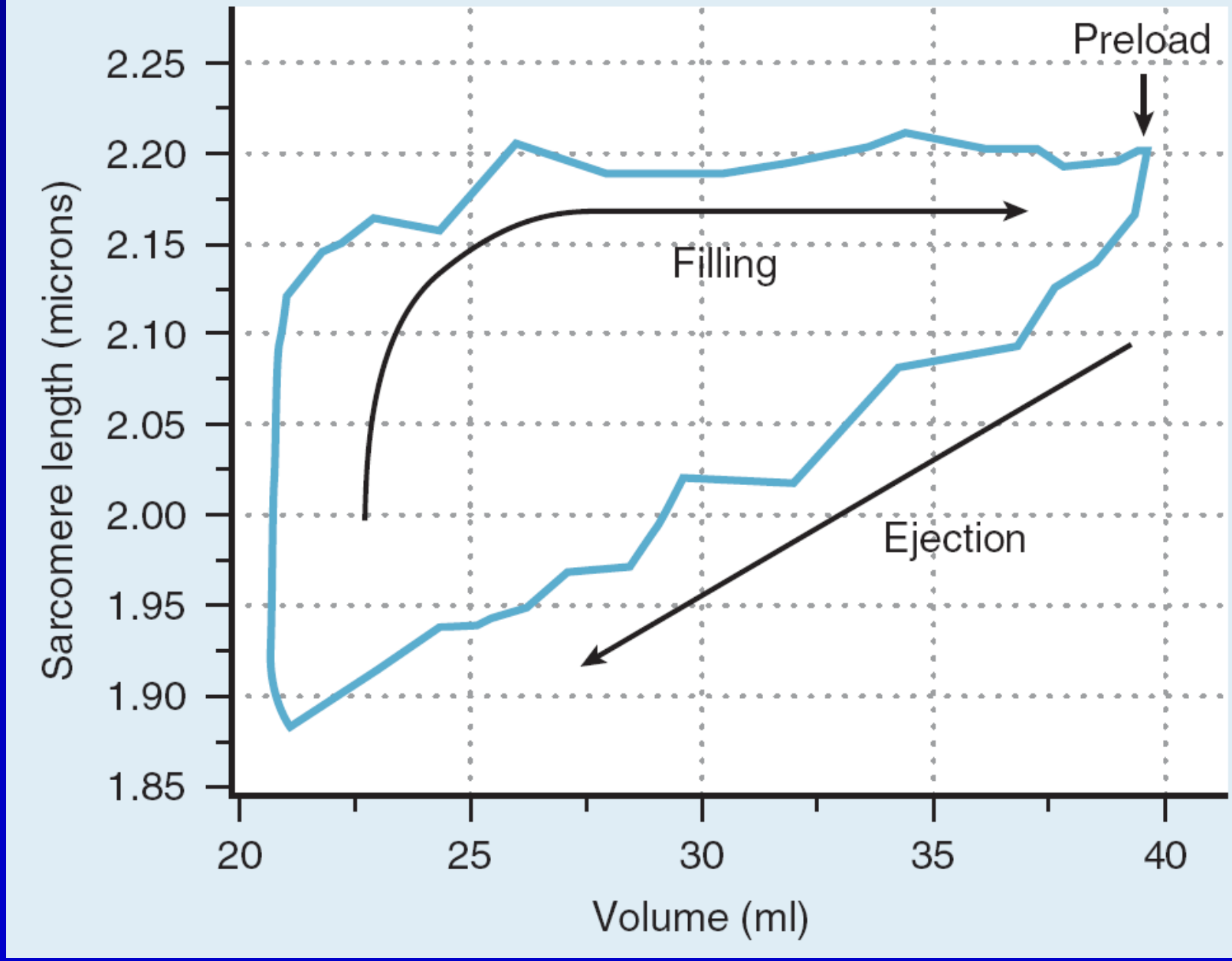


Guglieri M et al. Clin Chim Acta. 2005;361:54.

Fibrillin-1 in Fibrosis

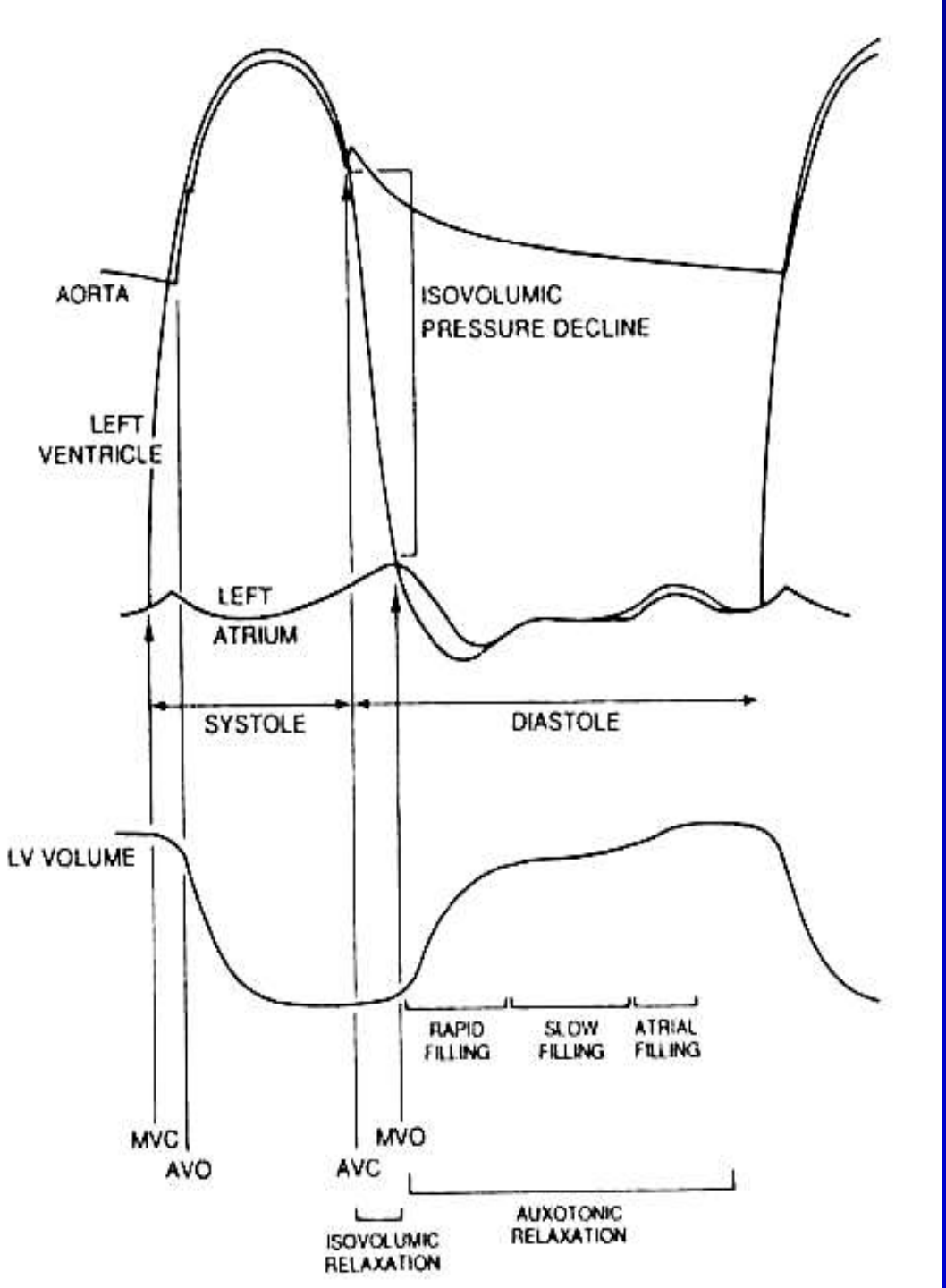


A J Physiol Heart Circul 2005



Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.

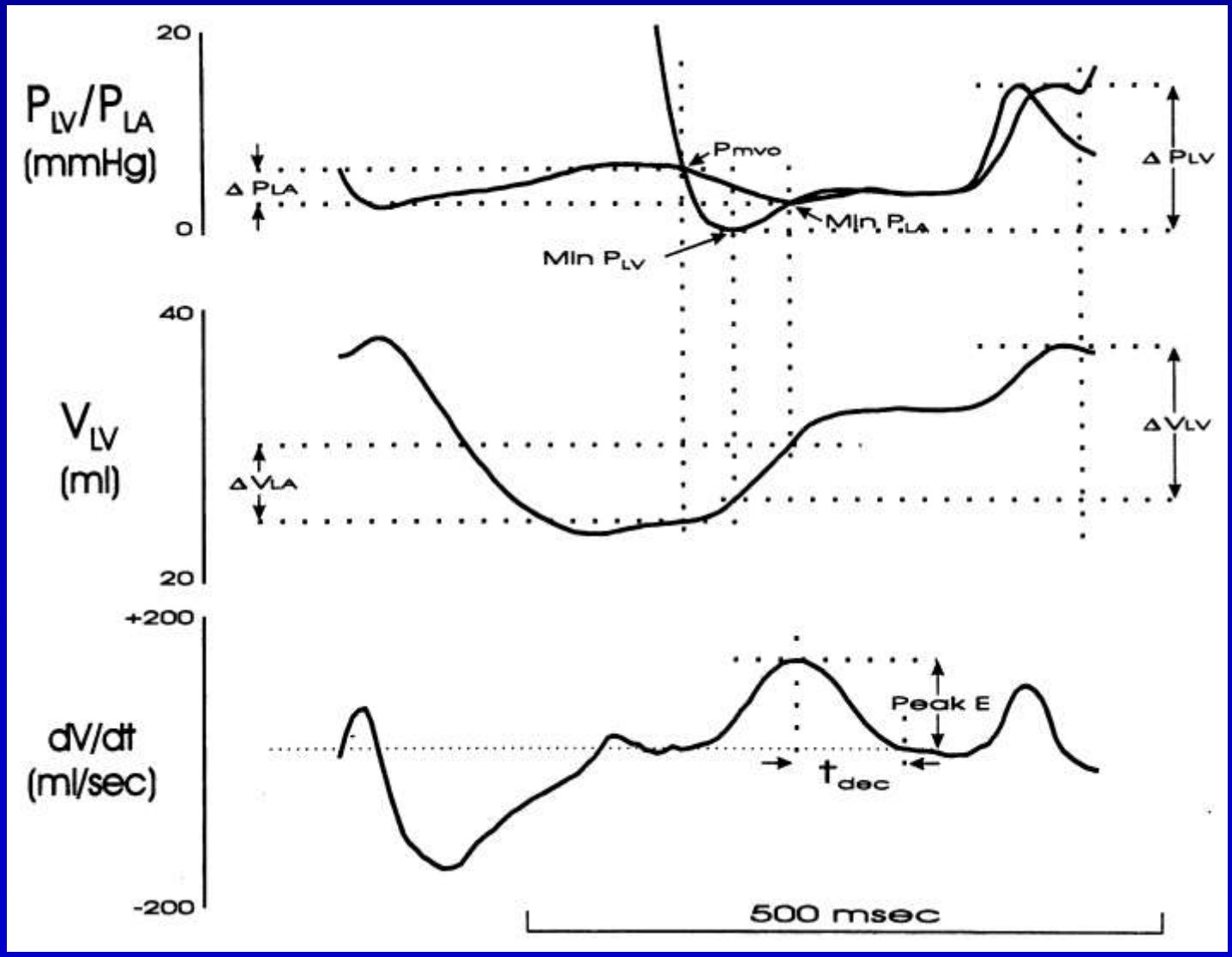
Diastolic Phases



Smith, Mikel, in Otto, 1997 from Zile MR. Echocardiography 1992;9:289.

Diastolic Pressure and Flow

Canine model with ultra-sonic crystals and micro-manometer pressures

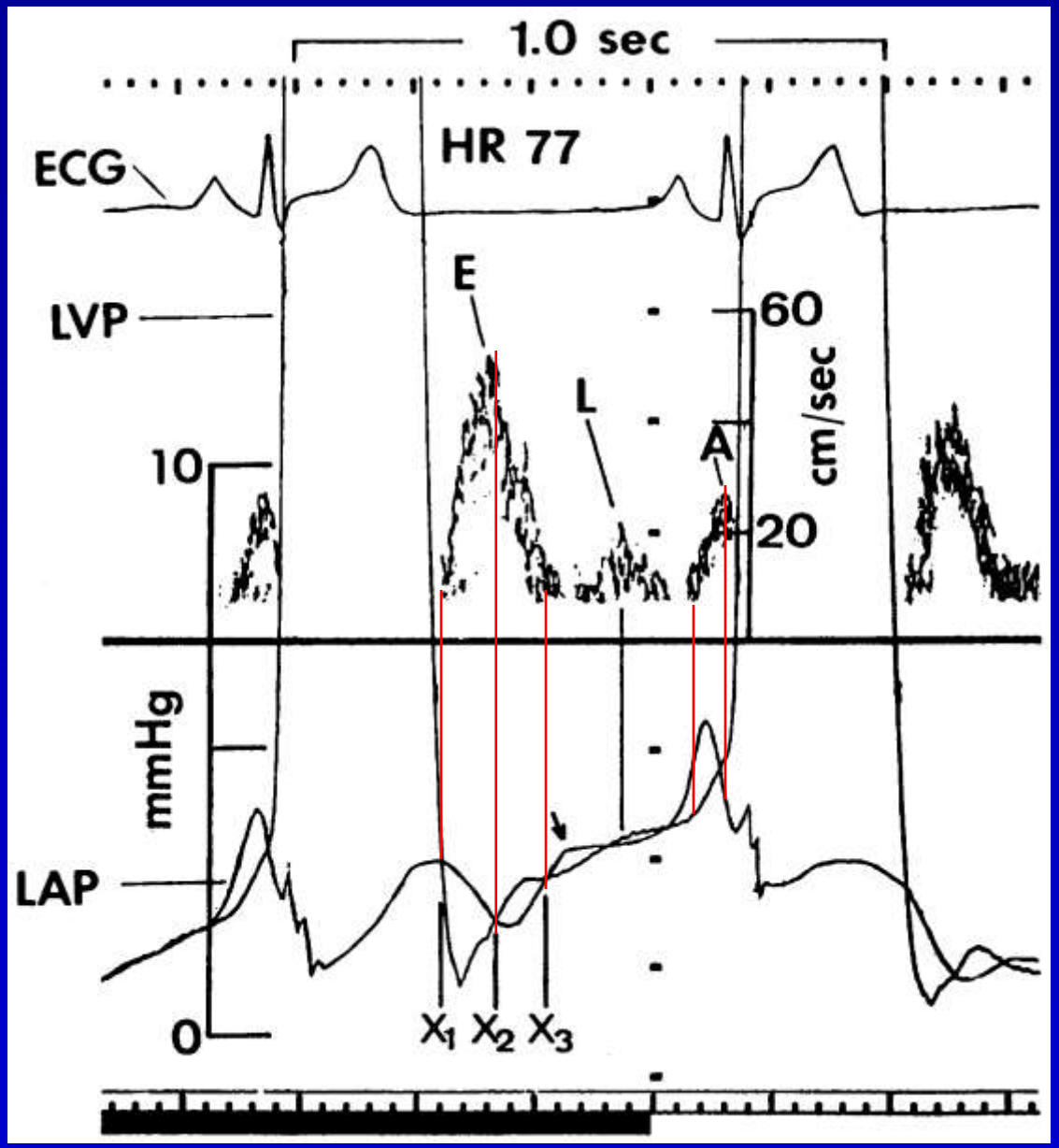


From Ohno M et al. Circulation 1994;89:2241

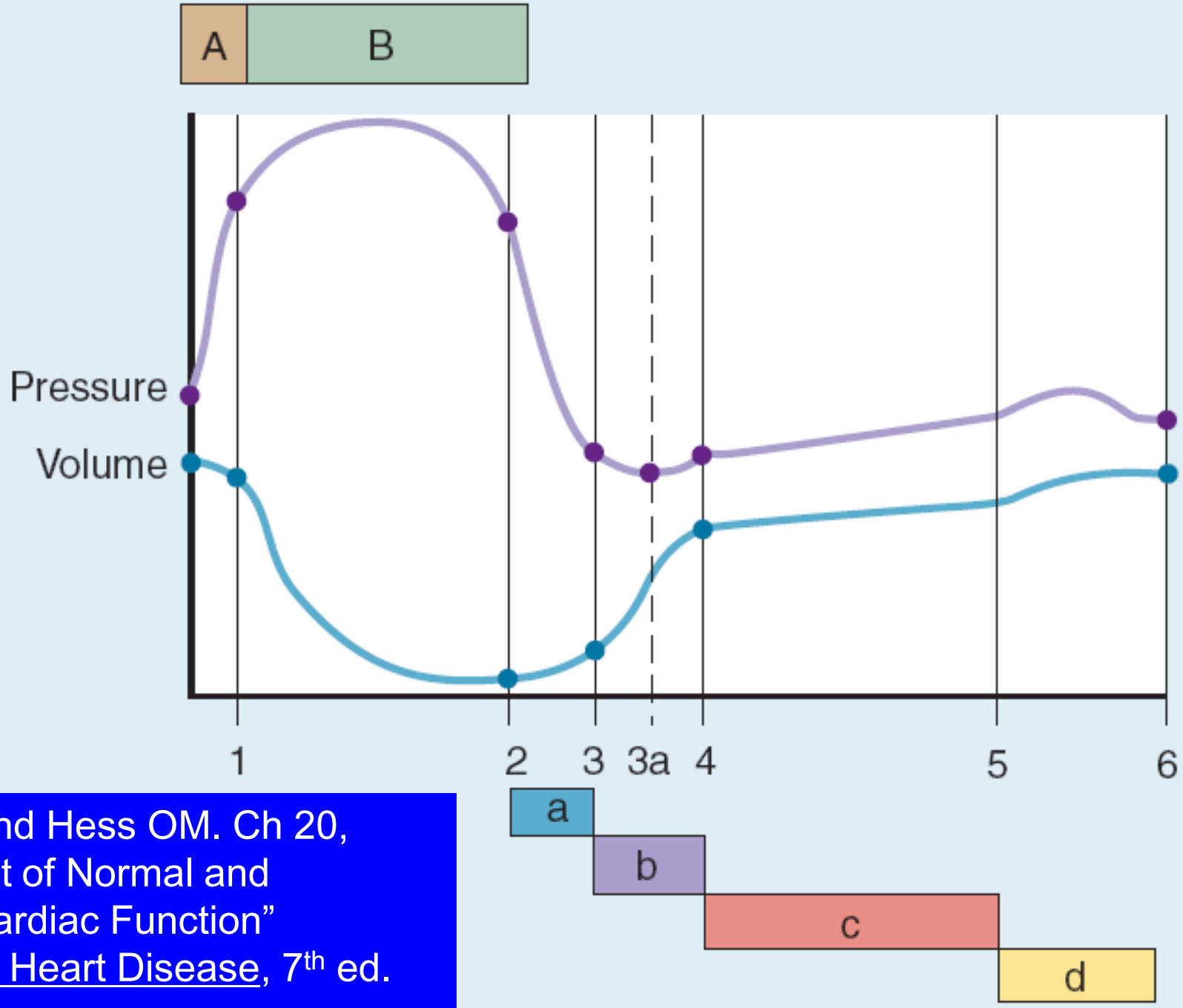
Diastolic Pressure and Flow

High fidelity LA and LV pressure and Doppler transmitral

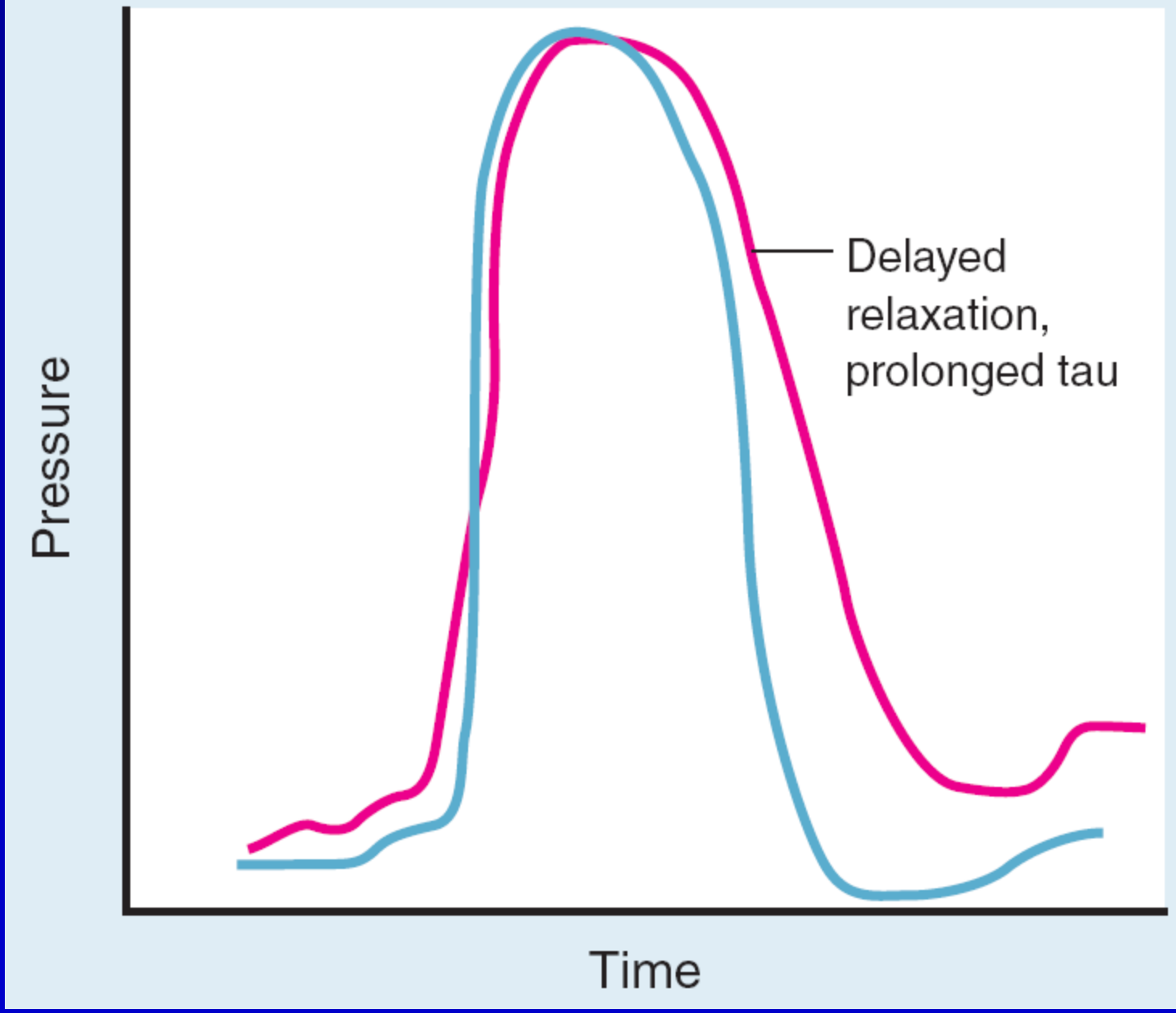
Closed chest canine



Courtois M et al.
Circulation 1988;78:661



Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.



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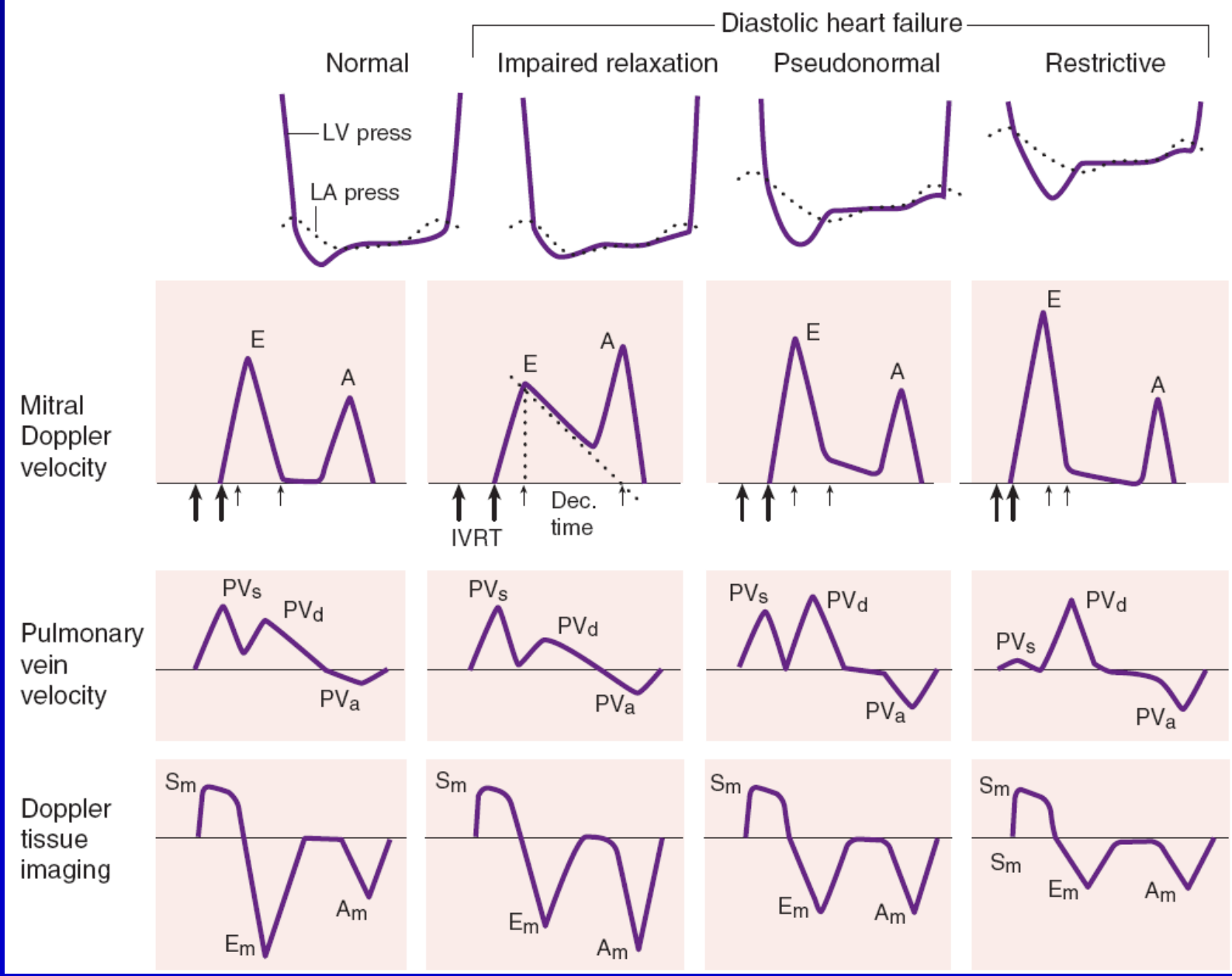

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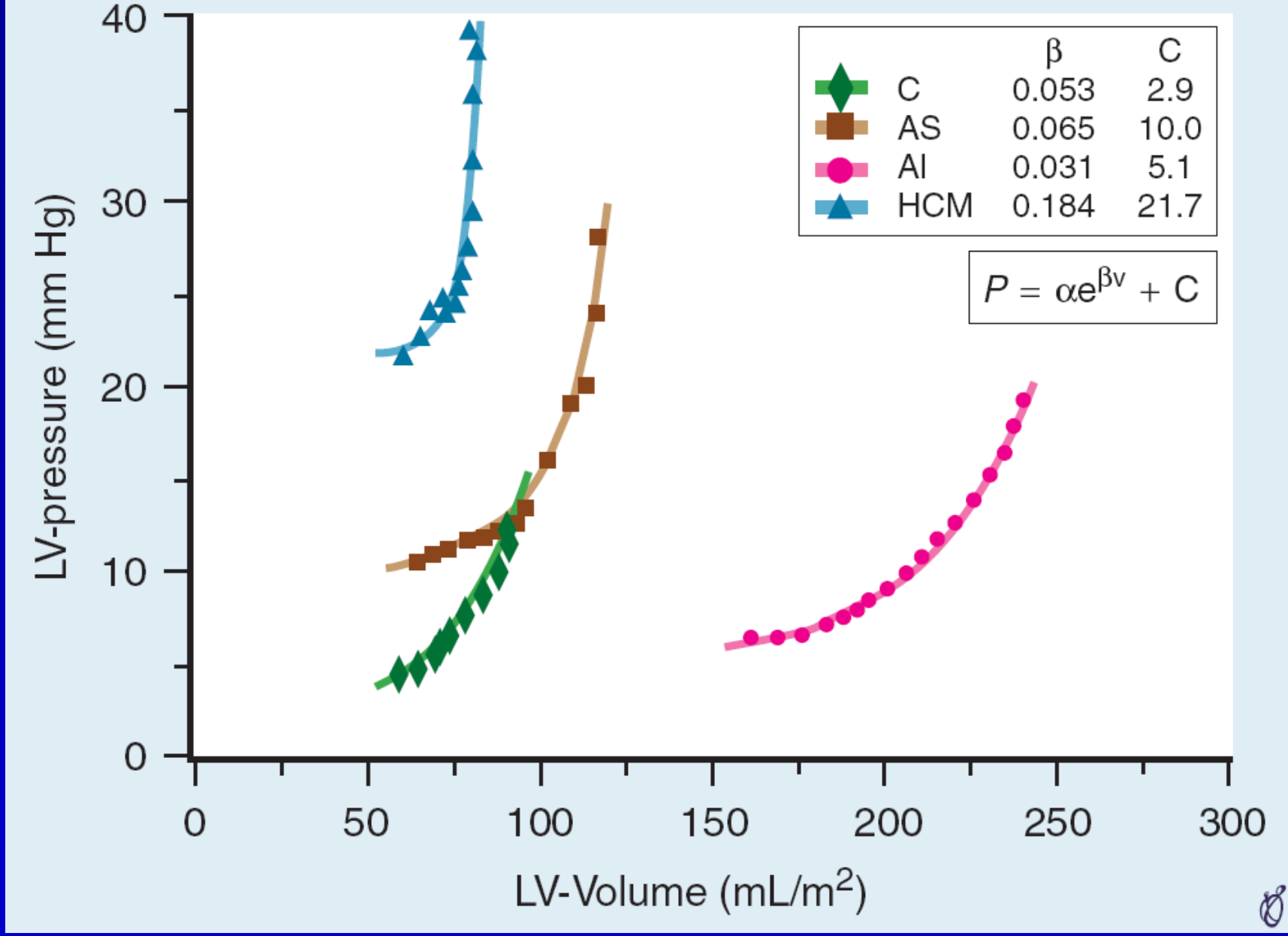

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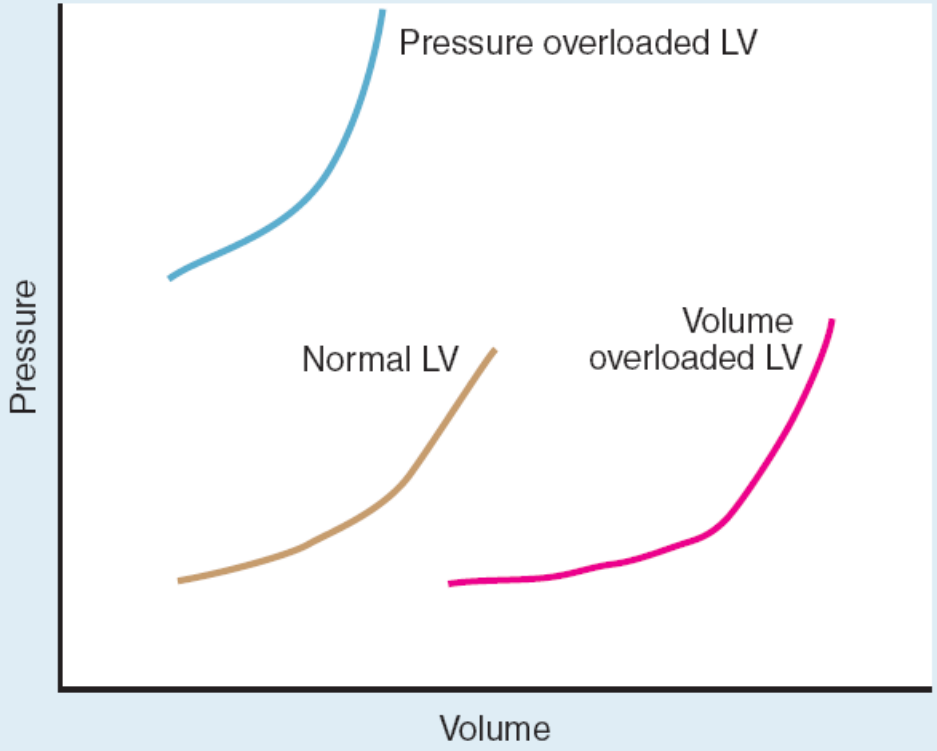
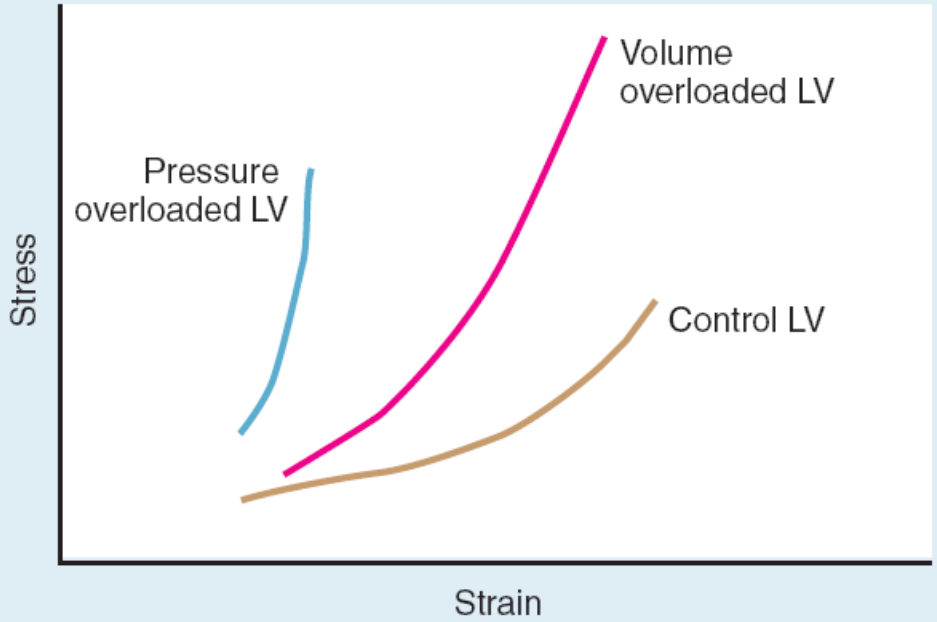




Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–3 Two Pathways of Ventricular Dilation and Increased Filling Pressure

Hemodynamic (Acute)

Dilation and increased end-diastolic pressure caused when increased venous return or decreased ejection increases end-diastolic volume. This form of dilation occurs when physiological (functional) signaling increases sarcomere length, which increases the heart's ability to perform work (Starling law of the heart)

Architectural (Chronic)

Dilation and increased filling pressures caused when hypertrophy increases cardiac myocyte length and alters passive muscle properties. By increasing wall stress, this growth response increases the energy demands of the heart and decreases cardiac efficiency, initiating a vicious circle that worsens heart failure. This form of dilation occurs when abnormal transcriptional (proliferative) signaling causes eccentric hypertrophy (systolic dysfunction), and it tends to progress (remodeling)

Adapted from Katz A: Ernest Henry Starling, his predecessors, and the "law of the heart." Circulation 106:2986, 2002.

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–5 Normal Values of Parameters of Left Ventricular Diastolic Filling Measured by Doppler Echocardiography

Parameters	Adults <41 yr	Adults >55 yr
Peak mitral flow velocity (E) (cm/sec)	76 ± 13	63 ± 11
Peak mitral filling rate (A) (cm/sec)	38 ± 8	52 ± 9
Mitral E/A	2.1 ± 0.6	1.3 ± 0.3
Mitral E deceleration time	184 ± 24	—
Mitral E deceleration rate (m/sec^2)	5.6 ± 2.7	—
Isovolumetric relaxation time (msec)	74 ± 26	—
Peak pulmonary venous AR wave (cm/sec)	18 ± 3	25 ± 5
Peak pulmonary venous S wave (cm/sec)	41 ± 10	60 ± 10
Peak pulmonary venous D wave (cm/sec)	53 ± 10	38 ± 10

E/A = E wave/A wave ratio.

Data from Little WC. Downes TR: Clinical evaluation of left ventricular diastolic performance. Prog Cardiovasc Dis 32:273, 1990; and Rakowski H, et al: Canadian consensus recommendations for the measurements and reporting of diastolic dysfunction by echocardiography. J Am Soc Echocardiogr 9:745, 754, 1996.

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–6 Left Atrial and Ventricular Function Influences on the Pulmonary Venous Flow Velocity Profile

Pulmonary Venous Wave	Left Atrial Function	LV Function
First systolic wave	Atrial relaxation	
Second systolic wave	Reservoir function Atrial compliance	LV contraction RV contraction
Early diastolic wave	Conduit function	Ventricular relaxation Ventricular chamber stiffness
Atrial reversal wave	Booster pump function Atrial compliance	Ventricular chamber stiffness

LV = left ventricular; RV = right ventricular.

Adapted from Tabata T, Thomas JD, Klein AL: Pulmonary venous flow by Doppler echocardiography: Revisited 12 years later. J Am Coll Cardiol 41:1243-1250, 2003.

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–8 Age-Related Differences in LV and Arterial Coupling in Patients with Dilated Cardiomyopathy

Parameters	Young Patients <35 yr	Intermediate-Aged Patients 35-50 yr	Older Patients >50 yr
Maximum + dP/dt (mm Hg/sec)	1011 ± 160	1170 ± 159	1147 ± 374
Stroke work (g-m/m^2)	19 ± 10	20 ± 10	19 ± 10
Pulse pressure (mm Hg)	26 ± 8	30 ± 11	38 ± 10
Pulse wave velocity (m/sec)	4.7 ± 0.4	6.5 ± 0.9	7.9 ± 0.6
Systemic vascular resistance (dyn-sec · cm^{-5})	1872 ± 789	2373 ± 762	2440 ± 770
Arterial compliance (ml/mm Hg)	1.33 ± 0.63	0.72 ± 0.40	0.51 ± 0.17

LV = left ventricular.

Adapted from Carroll JD, Shroff S, Arand P, et al: Arterial mechanical properties in dilated cardiomyopathy. J Clin Invest 87:1002-1009, 1991.

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 19–5 Some Indices of Diastolic Function

Isovolumic Relaxation
(–)dP/dt_{max} (Fig. 19–28)
Aortic closing–mitral opening interval
Peak rate of LV wall thinning
Time constant of relaxation (τ)
Early Diastolic Filling
Relaxation kinetics on ERNA (rate of volume increase)
Early filling phase (E phase) on Doppler transmitral velocity trace
Diastasis
Pressure-volume relation indicates compliance
Atrial Contraction
Invasive measurement of atrial and ventricular pressures
Doppler transmitral pattern (E to A ratio)

A = atrial contraction phase; E = early filling phase; ERNA = equilibrated radionuclide angiography; LV = left ventricular.

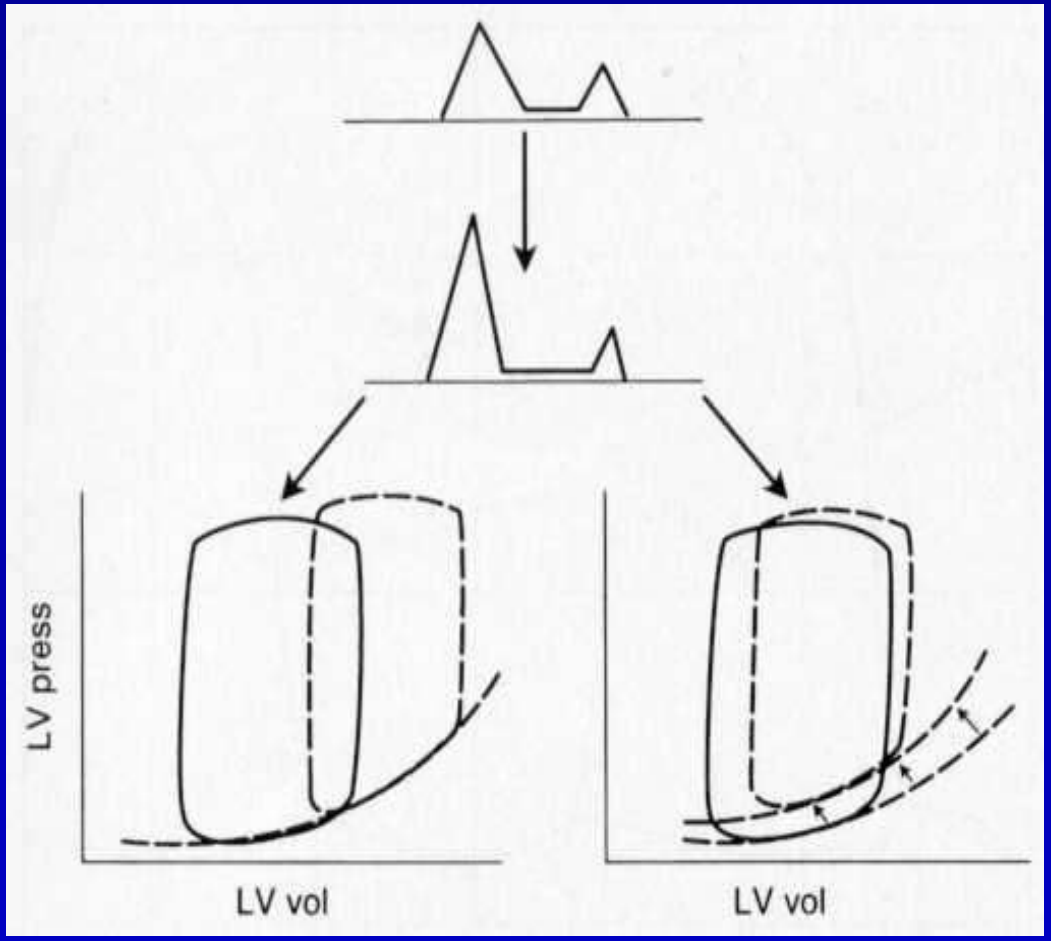
Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.

Assessment of Diastolic Function

- M-mode Echo:
  - chamber sizes
  - mitral and LV motion
  - aortic root motion
- 2-D (B-mode) Echo:
  - chamber sizes and wall thickness
  - mitral and LV motion
  - aortic root motion
  - atrial volume change
  - interatrial septal shape and motion
- Doppler assessment

Doppler Assessment of Diastole

- **Transmitral flow assessment**
- Isovolumic relaxation time
- Pulmonary venous flow assessment
- Flow propagation velocity
- Pulse transit time
- Tissue Doppler imaging



Normal LVIT Pattern

Decreased Operative Compliance (increase E and
short E-deceleration)

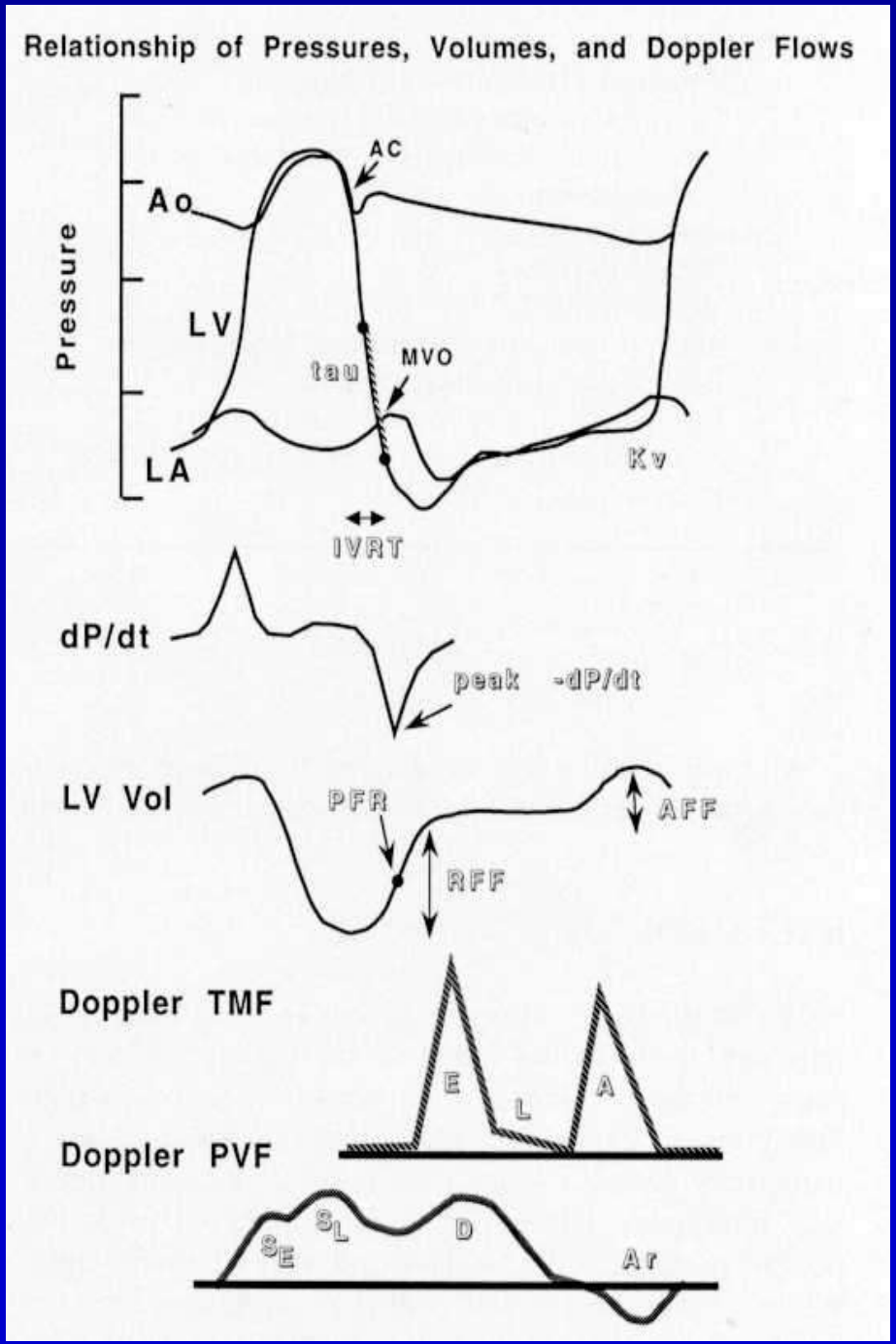
Diastolic Pressure-Volume Relation and LVIT Pattern

Normal diastolic pressure-volume relation with increased volume

Abnormal diastolic pressure-volume relation with no change in volume

Nishimura, JACC 1997; 30:8

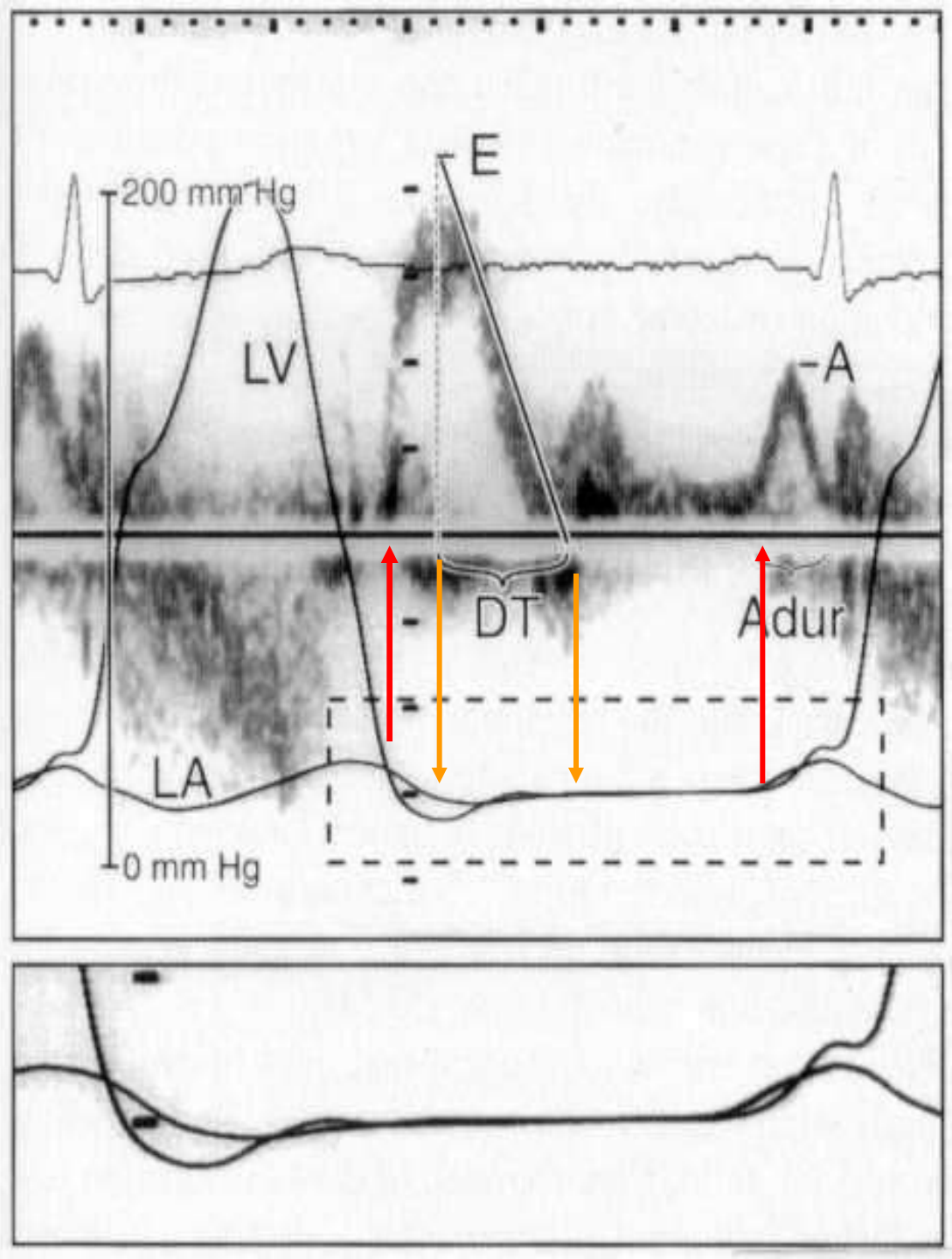
Diastolic Patterns of Pressure, Volume, and Flow



Smith, Mikel, in Otto, 1997

LVIT Velocity Measurements

E - peak E velocity
A - peak A velocity
DT - time from peak E to zero
Decel slope – more dependent on peak E height
A dur - duration of A wave



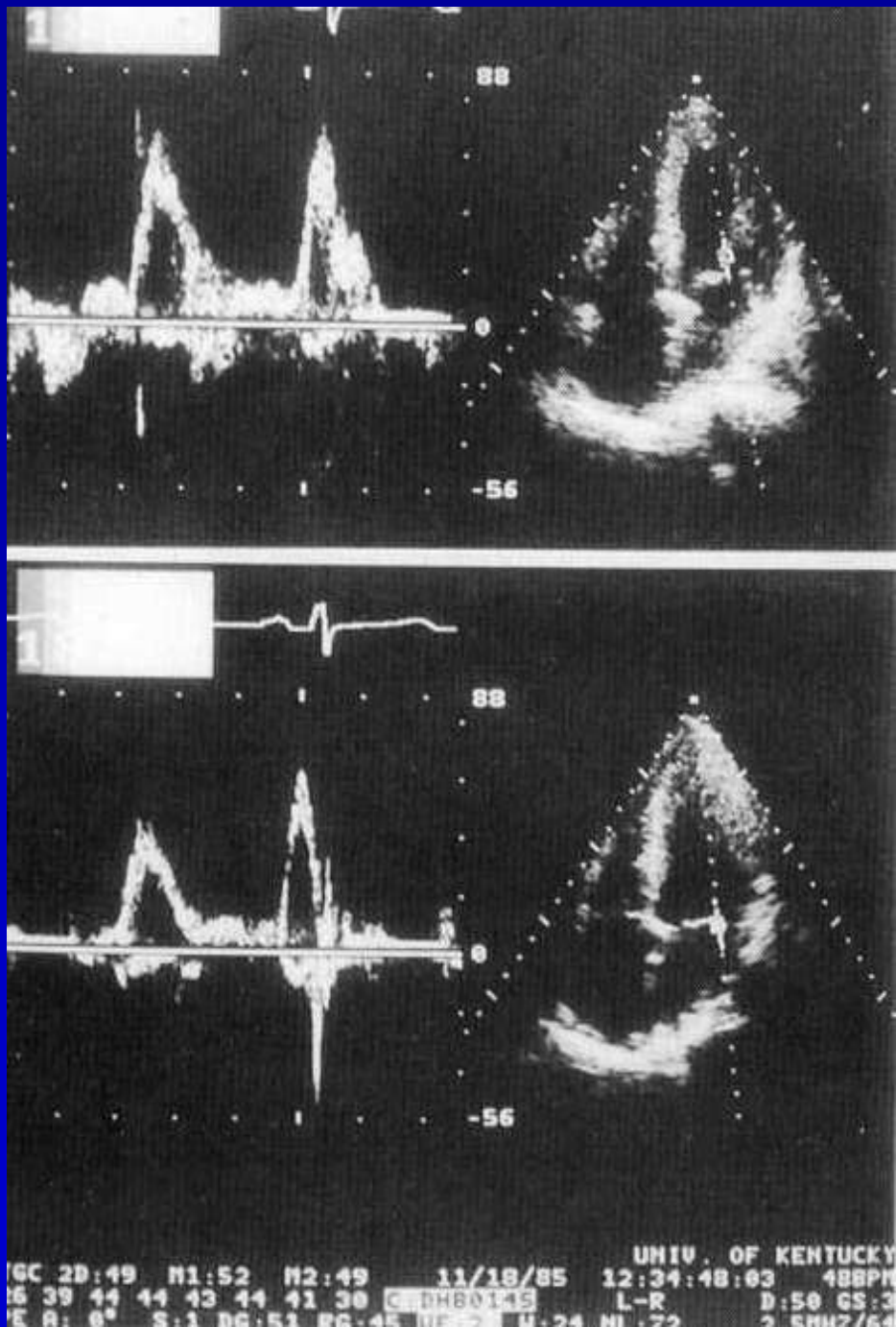
Nishimura, JACC 1997; 30:8

Technical Aspects of LVIT Pattern

Leaflet Tips

- Pulsed wave preferred
- Apical 4 (or 2 or LA)
- Sample volume at mitral leaflet tips
- Modal (darkest) velocity

Mitral Annulus



Smith, Mikel, in Otto, 1997

LVIT Flow Pattern

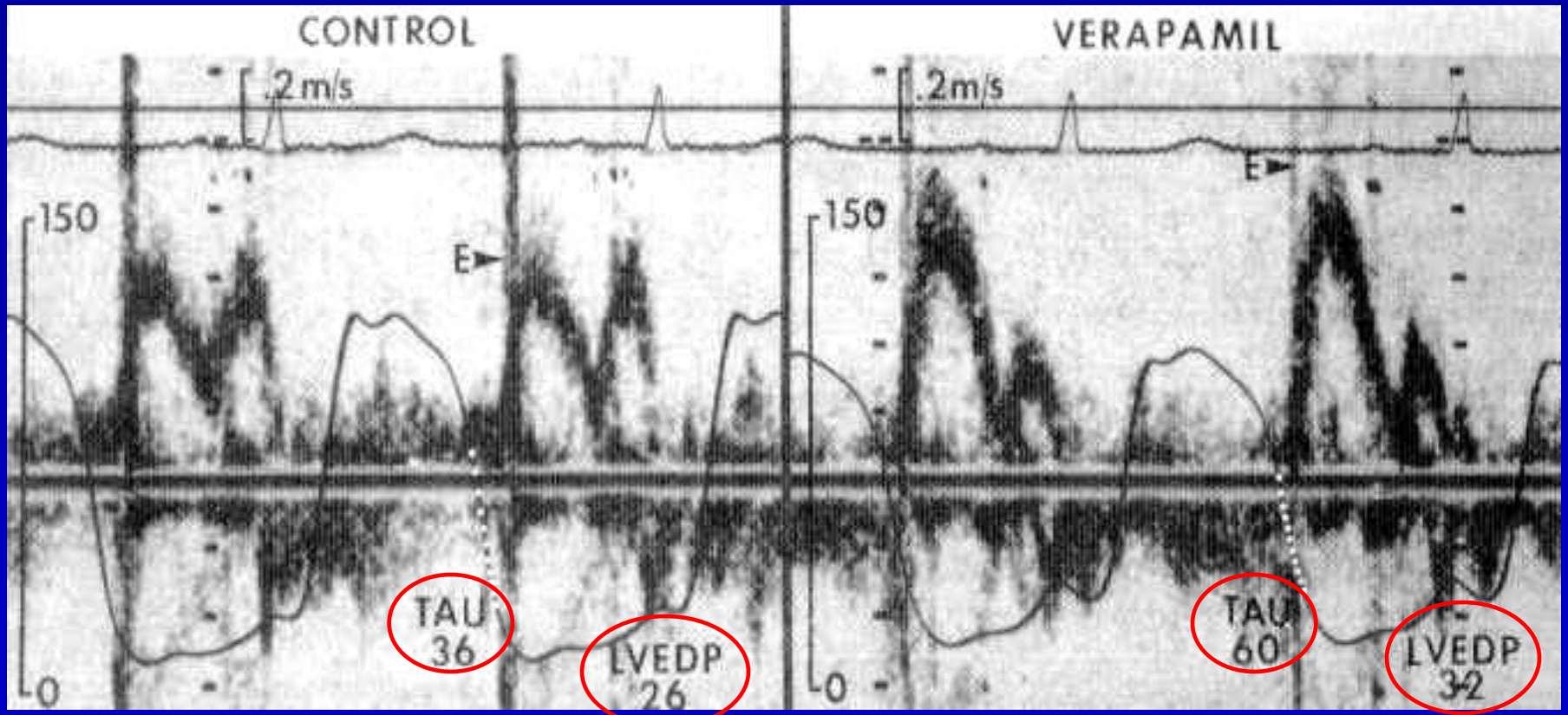
- Normal: E 70-100 cm/s, A 45-70 cm/s, E/A 1.0-1.5, DT 160-220 msec
- Older: lower E, higher A, lower E/A, longer DT
- Arrhythmia: Faster HR and longer PR interval- lower E, higher A, merge at >100; afib - no A, variable E
- Preload: decrease causes decrease in E wave and no change of A wave
- Systolic function: increase in end-systolic volume (systolic dysfunction or high afterload) lowers E and slows DT
- Atrial function: atrial systolic dysfunction gives low A wave
- Respiration: inspiration reduces E by 5-10%, no change in A

Factors Affecting Mitral E/A Ratio

- Increased:
  - Slow heart rate
  - Elevated LA pressure
  - High LV elastic recoil
  - Young age (phys S3)
  - Restrictive hemodyn
  - Severe AR
  - Atrial mechanical fail
  - Small LVESV
- Decreased
  - Abnormal LV relaxation
  - Increased aortic pressure
  - Increased PR interval
  - Tachycardia
  - Asynchronous LV relaxation

Pai RG. Clin Cardiol 1996;19:277

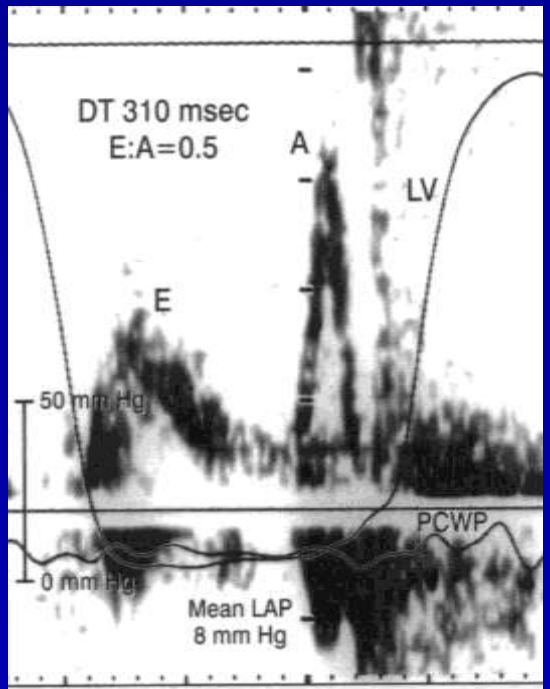
Limitation of LVIT Doppler pattern in diastolic function

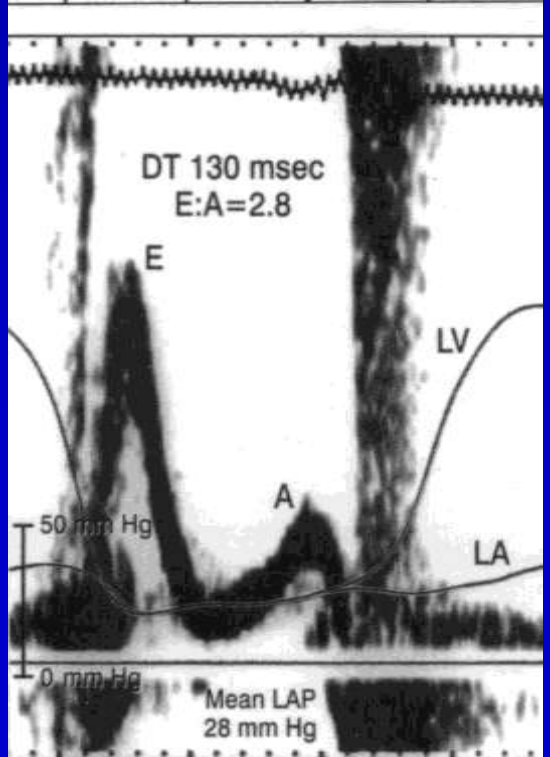


Deterioration of diastolic function with benign-appearing LVIT flow

Nishimura, JACC 1997; 30:8

Abnormal Transmitral (LVIT) Filling Patterns





Nishimura, JACC 1997; 30:8

Abnormal Relaxation
- advanced age
- low preload
- systolic dysfunction
- tachycardia
- long PR
- ischemia
- pulmonary htn

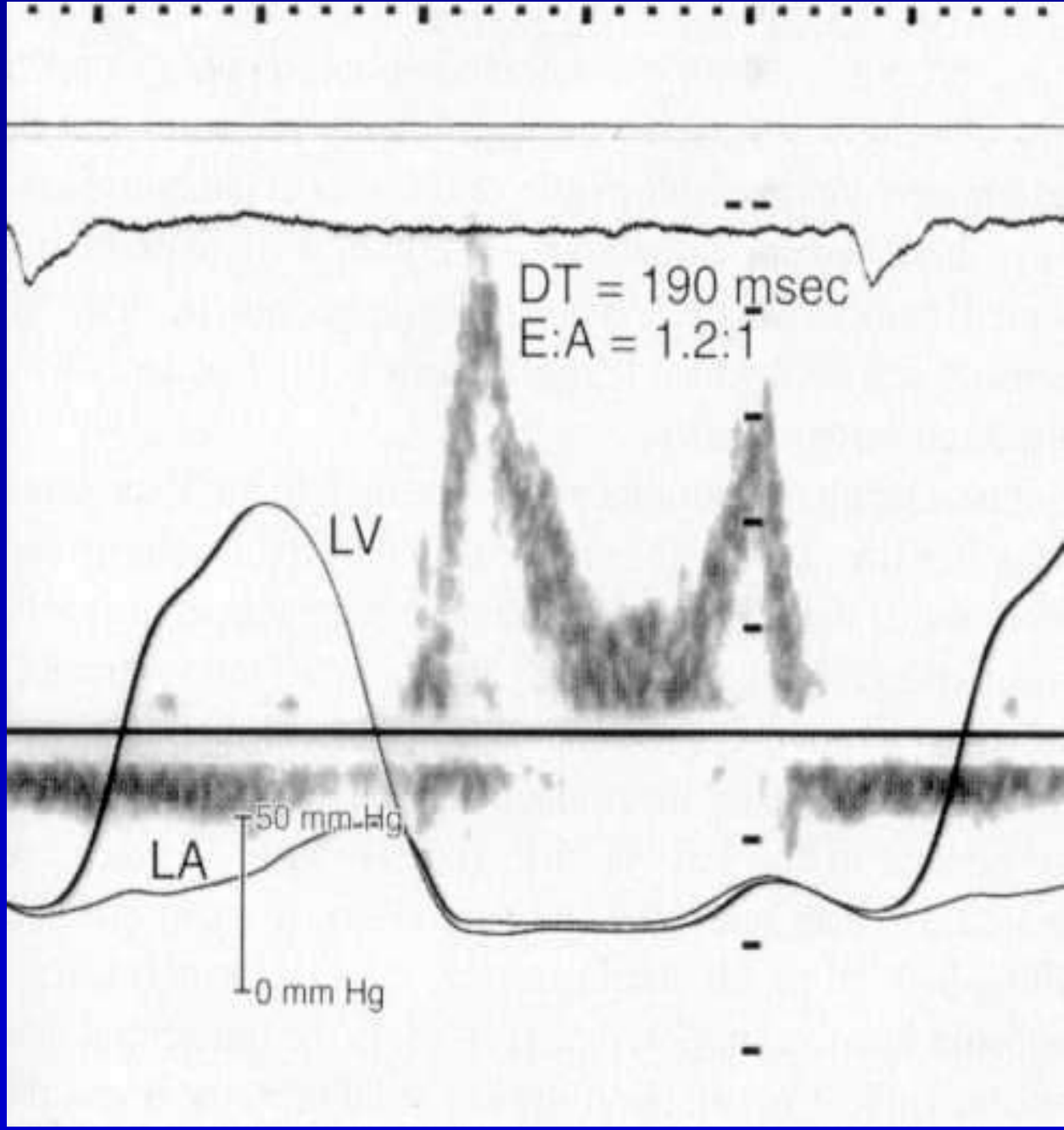
Restrictive Filling
patient with dilated cardiomyopathy

LVIT Doppler Pseudo-normalization

62 year-old man, dilated Cardiomyopathy:

Prolonged LV relaxation, tau = 68 msec

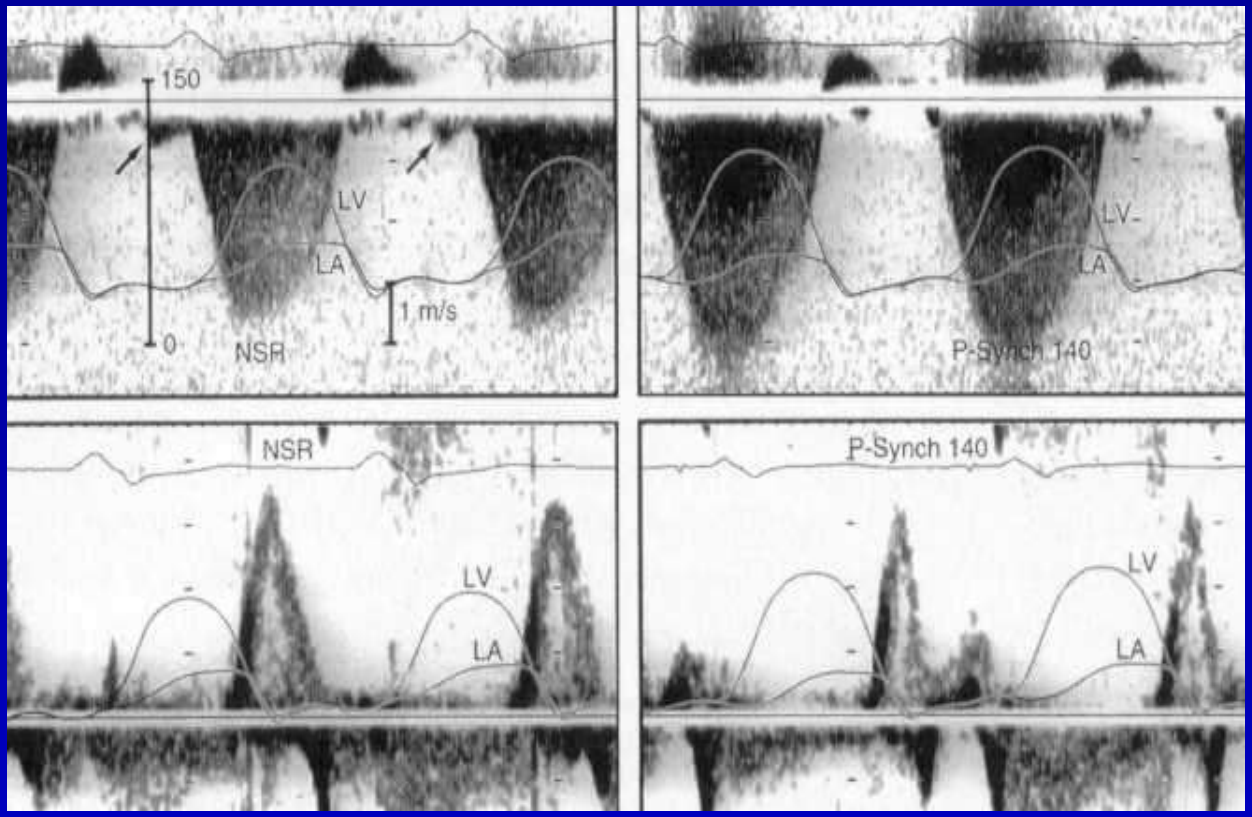
Elevated LA pressure 32mmHg



Nishimura, JACC 1997; 30:8

CW Doppler of MR

PW Doppler LVIT (not simultaneous)



PR interval and Diastole

Baseline:

- first degree AV block
- diastolic MR and
- E-A superimposition

AV sequential pacing:

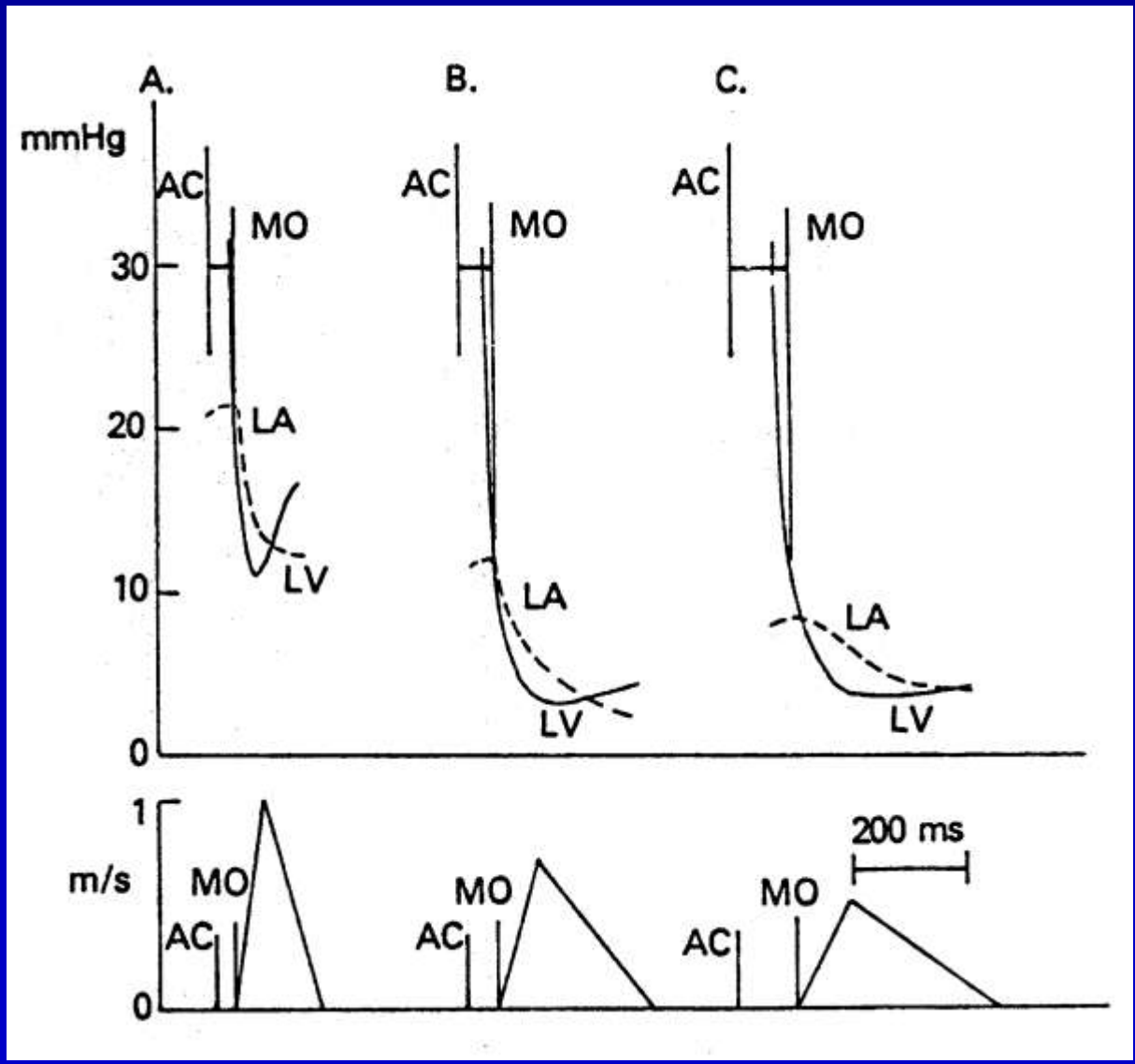
- PR interval normal
- no diastolic MR
- forward SV increase 40%

Nishimura, JACC 1997; 30:8

Doppler Assessment of Diastole

- Transmitral flow assessment
- **Isovolumic relaxation time**
- Pulmonary venous flow assessment
- Flow propagation velocity
- Pulse transit time
- Tissue Doppler imaging

Isovolumic Relaxation Time



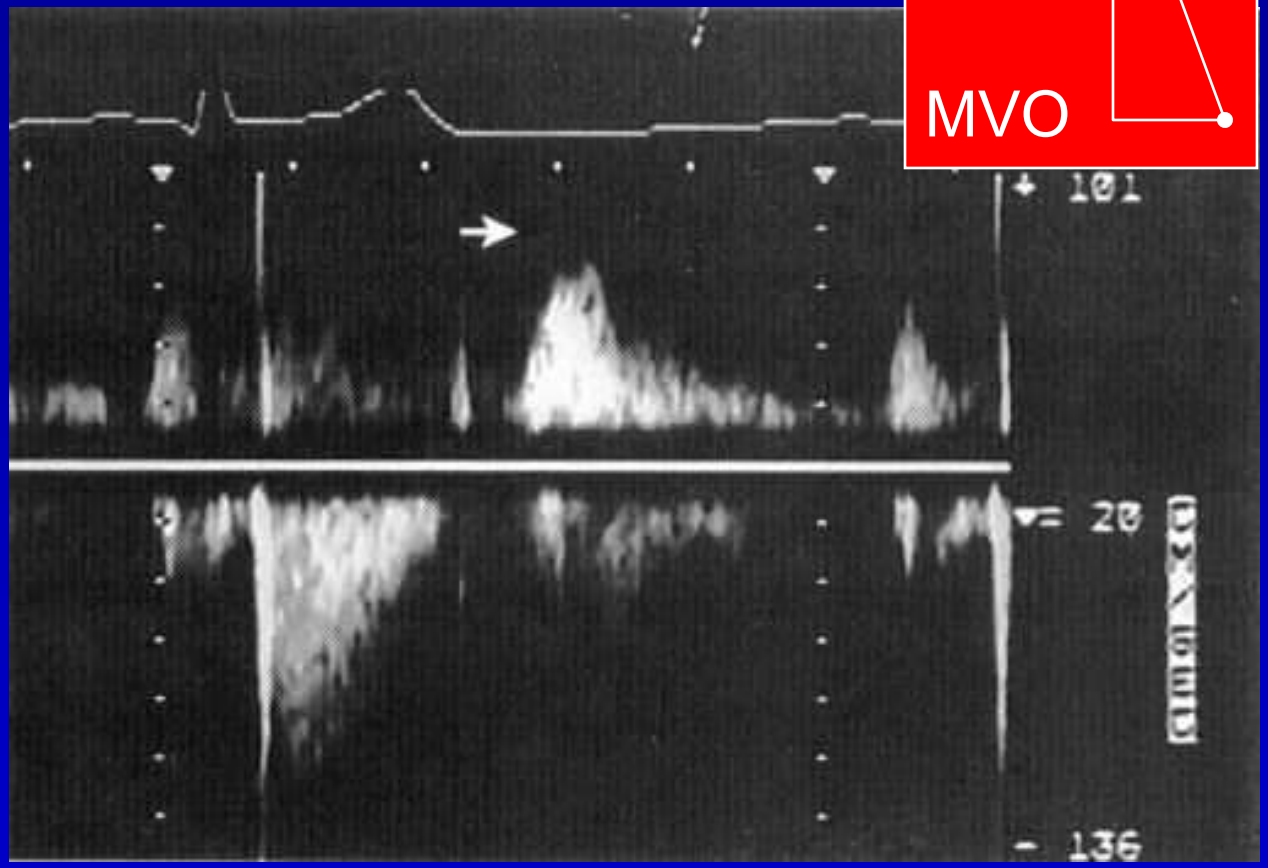
From Appleton CP et al. Echocardiography 1992;9:437

Isovolumic Relaxation Time

Time from aortic closure to mitral opening

From phono S2 to mitral opening on M-mode

Doppler method:
Apical five-chamber view
CW Doppler
Directed between aortic outflow and mitral inflow

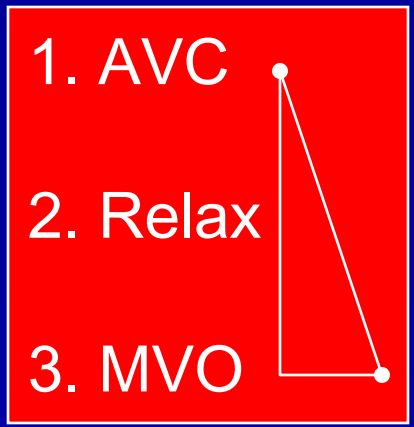


Normal 65 msec +/- 20

Short IVRT: restrictive cardiomyopathy
restrictive filling pattern
Long IVRT: advanced age, impaired relaxation

Smith, Mikel, in Otto, 1997

Isovolumic Relaxation Time



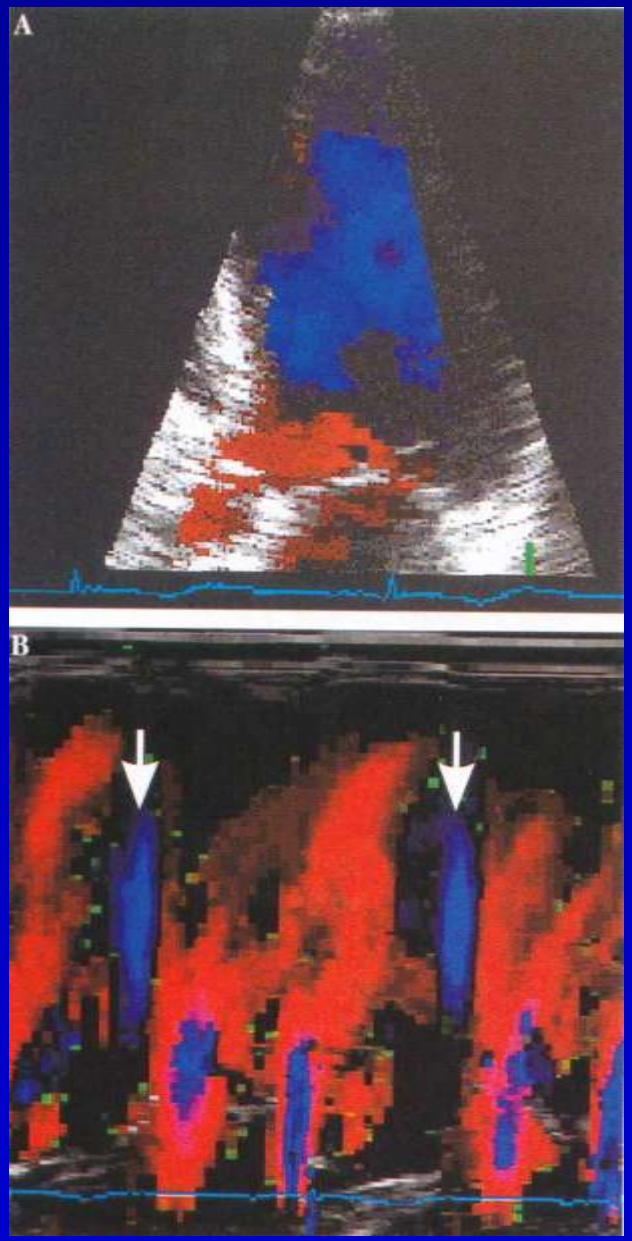
- Increased by
  - Abnormal LV relaxation (2)
    - Ischemia, infarction, hypertrophy, DM
  - Elevated aortic pressure (1)
  - Asynchrony of LV relaxation (LBBB, Paced, HCM) (2)
  - Aging (1,2)
- Decreased by
  - Elevated LA pressure (3)
  - Tachycardia (2)
  - Elevated sympathetic tone, catecholamines (2)
  - Smaller LV end-systolic volume (1)

Pai RG. Clin Cardiol 1996;19:277

Intraventricular flow during Isovolumic Relaxation

Abnormal flow from apex to base during IVRT in patient with anterior MI and apical wall motion abnormality.

Normally flow is from base to apex.



Edvardsen et al, JASE 1999; 12:801

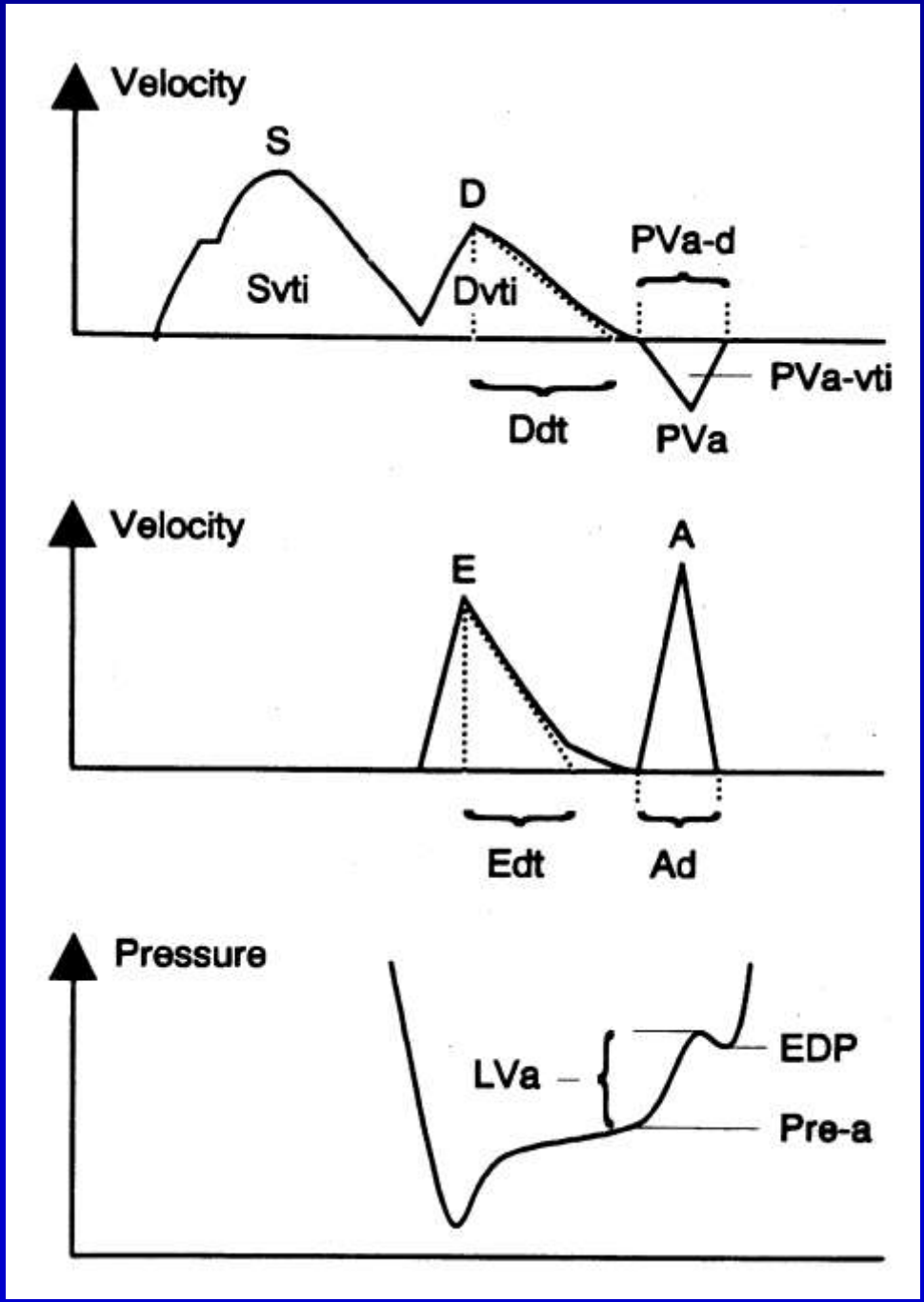
Doppler Assessment of Diastole

- Transmitral flow assessment
- Isovolumic relaxation time
- **Pulmonary venous flow assessment**
- Flow propagation velocity
- Pulse transit time
- Tissue Doppler imaging

Pulmonary Venous Flow

- Technique: TTE – right upper pulmonary vein, 5-10 mm from orifice
- Waves:
  - systolic usually dominant (S, 40-60 cm/s)
    - early – atrial relaxation
    - late – descent of MV annulus
  - diastolic (D, 35-45 cm/s, coincides with MV E wave but 50 msec later, from ventricular relaxation)
  - atrial reversal (Ar, 22-32 cm/s, duration 137msec, larger with high atrial afterload and preserved atrial systolic function)
- Tachycardia - S and D waves may merge

Pulmonary Venous Flow



From Rossvoll O et al. (Hatle)
J Am Coll Cardiol
1993:21:1687

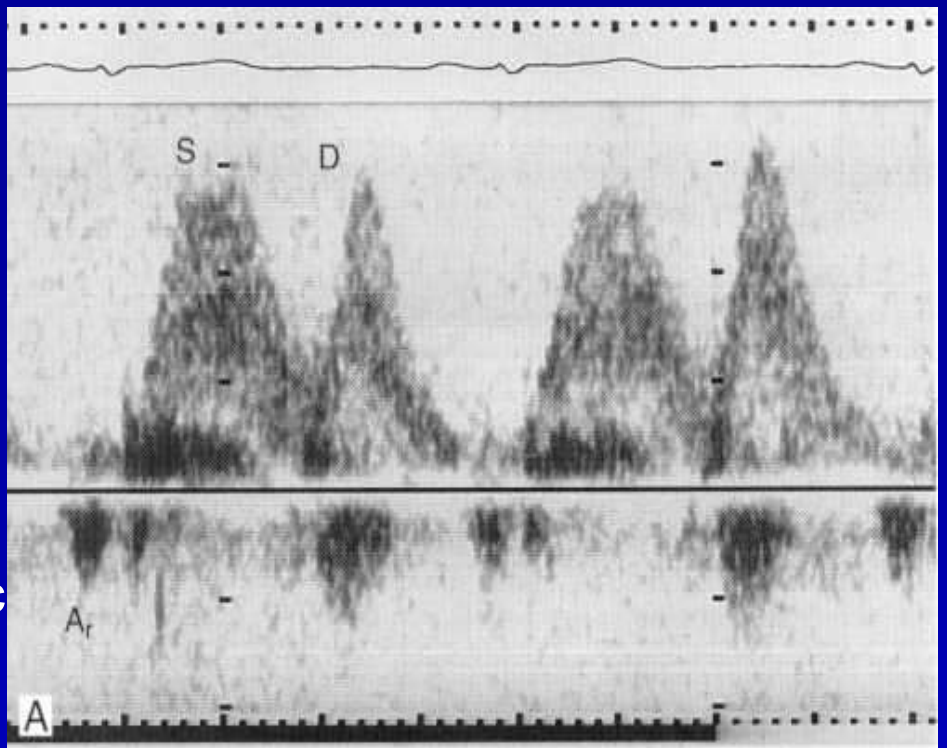
Pulmonary Venous Flow Pattern

- LV preload and systolic and diastolic function
  - Increased LA pressure - lower S if LV systolic dysfunction, (more S if LV systolic function is preserved)
  - Impaired relaxation – larger S and lower D, corresponding to lower MV E
  - Pseudonormal – lower S and dominant D wave and larger Ar wave (lower LV compliance)
  - Restrictive – low S and large D and rapid D deceleration, Ar is variable
- Age increases systolic dominance and maybe Ar
- Mitral regurgitation* reduces S wave, reverses if severe MR
- Large ASD causes single continuous antegrade wave and diminished AR wave**

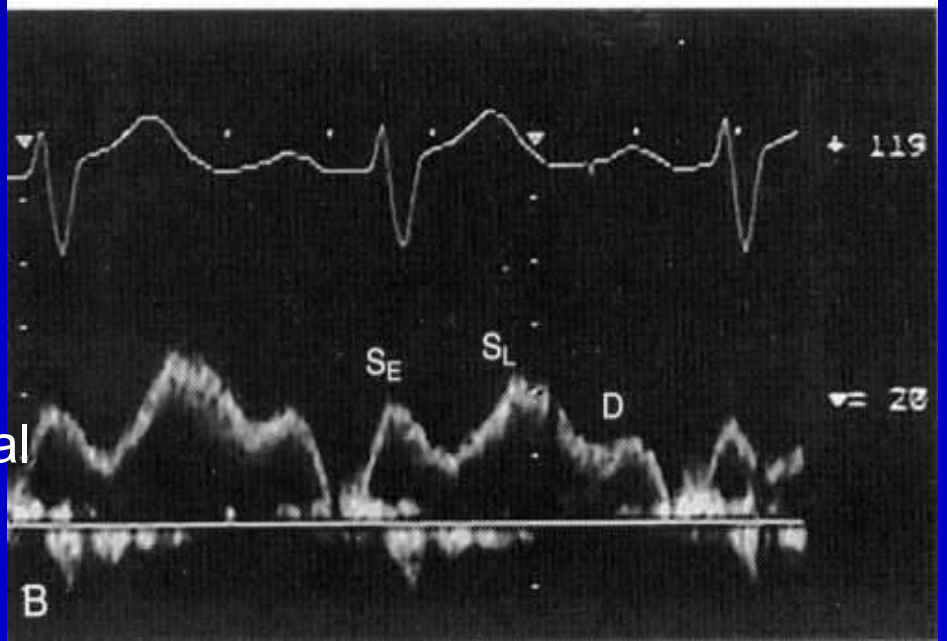
*Rossi A, et al. J Am Soc Echocardiogr 2001;14:562
**Saric M, et al. J Am Soc Echocardiogr 2001;14:386

Normal Pulmonary Vein PW Doppler Patterns

S - systolic
D - diastolic
SE - early systolic atrial relaxation
SL - late systolic descent of MV annulus
Ar - atrial reversal
Si - systolic integral
Di - diastolic integral



Transthoracic

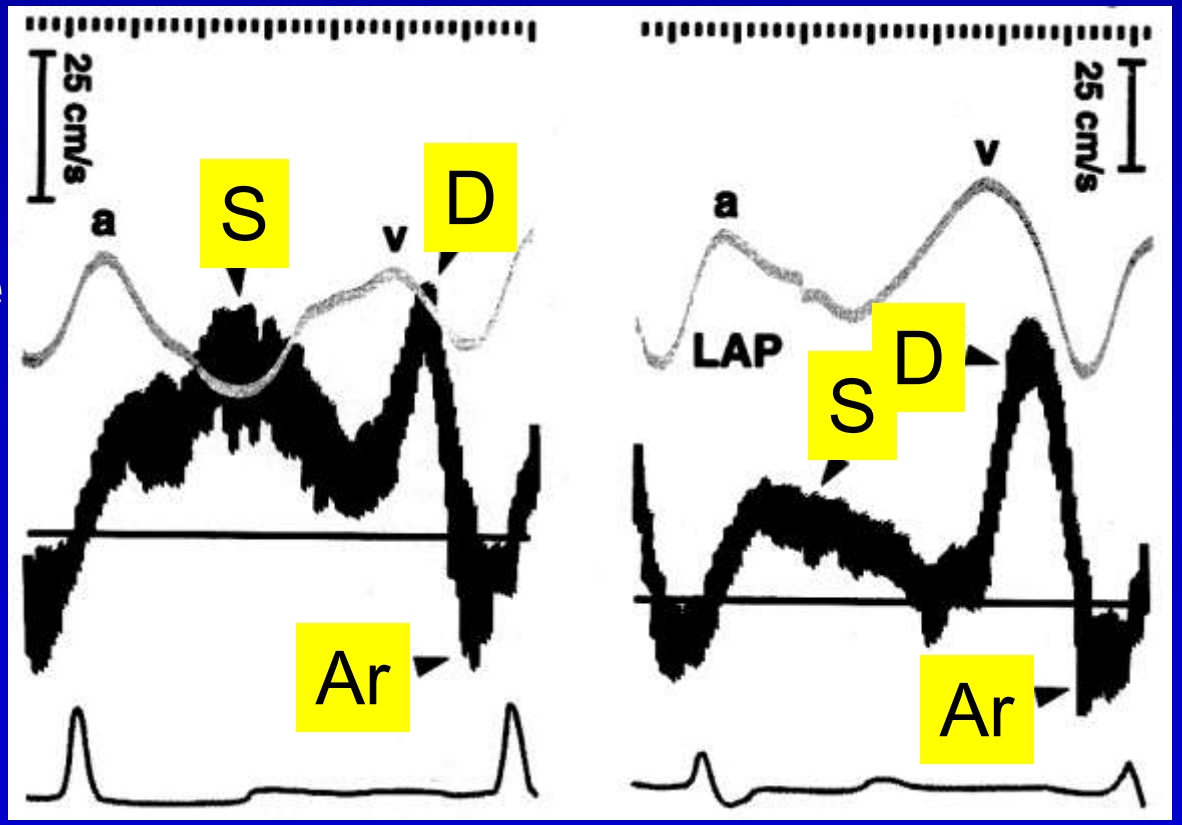


Transesophageal

Smith, Mikel, in Otto, 1997

Pulmonary Venous Flow and LA pressure

With higher LA pressure, the S wave is lower



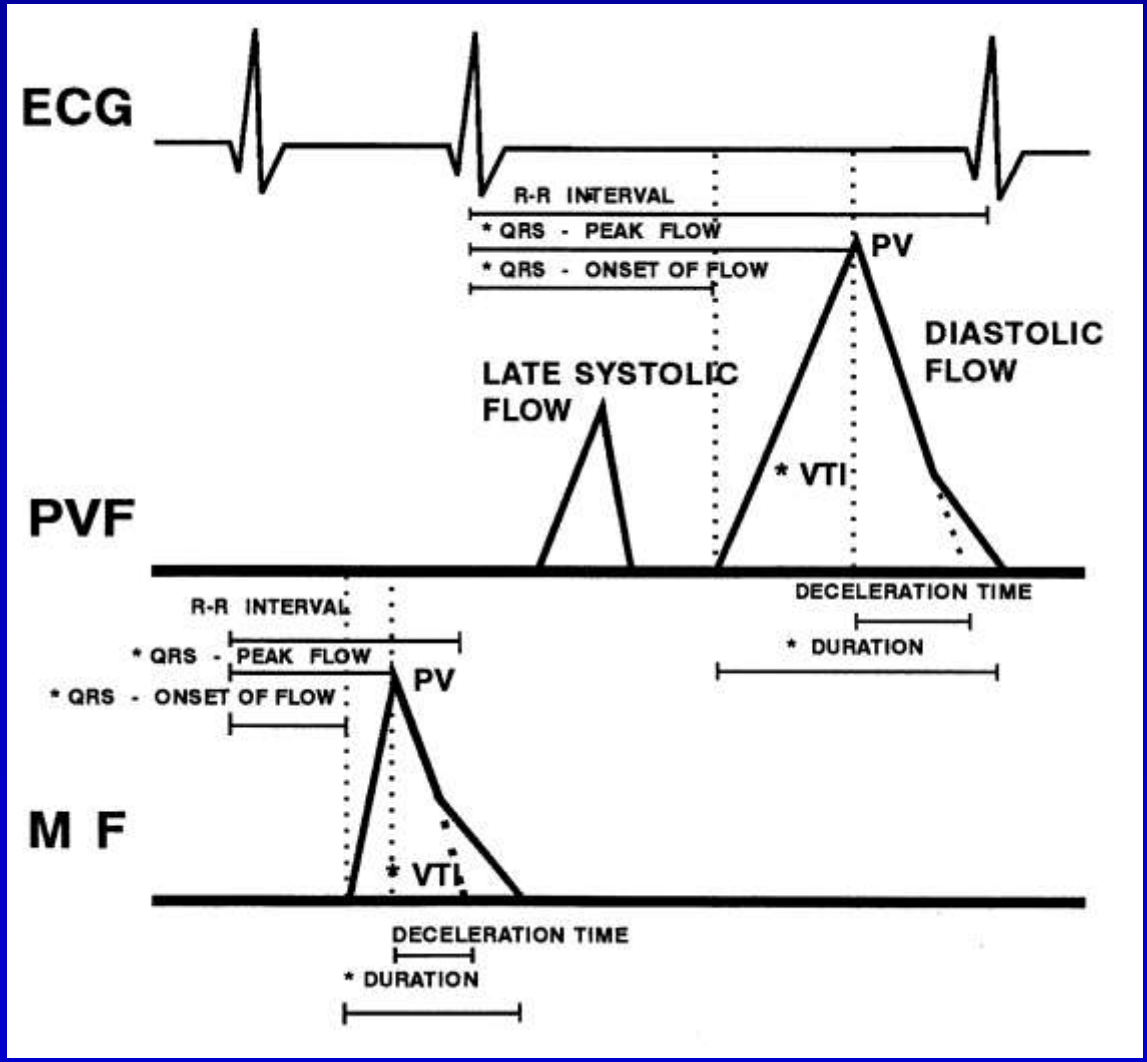
Kuecherer HR et al. Circulation 1990;82:1127

Pulmonary Venous Doppler and LV Diastolic Pressure

- 78 patients with chronic atrial fibrillation
  - 35 study group
  - 23 test group
- Wedge pressure simultaneous or very close in time to echo-Doppler
- Mitral and pulmonary vein flow patterns
  - Pulmonary venous diastolic measurements
  - Transmitral E wave measurements

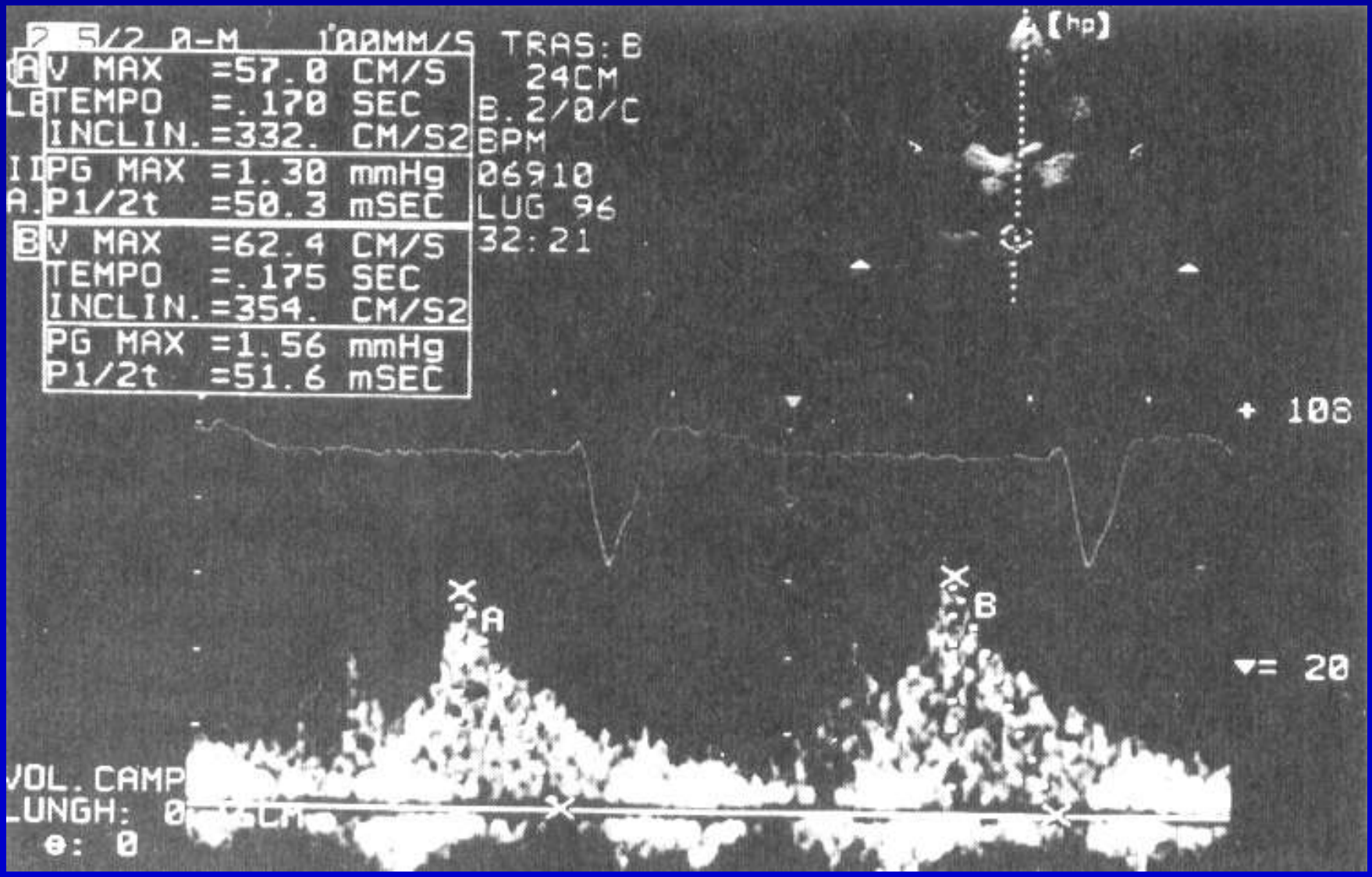
Chirillo F et al. J Am Coll Cardiol 1997;30:19

Pulmonary Venous Doppler and LV Diastolic Pressure

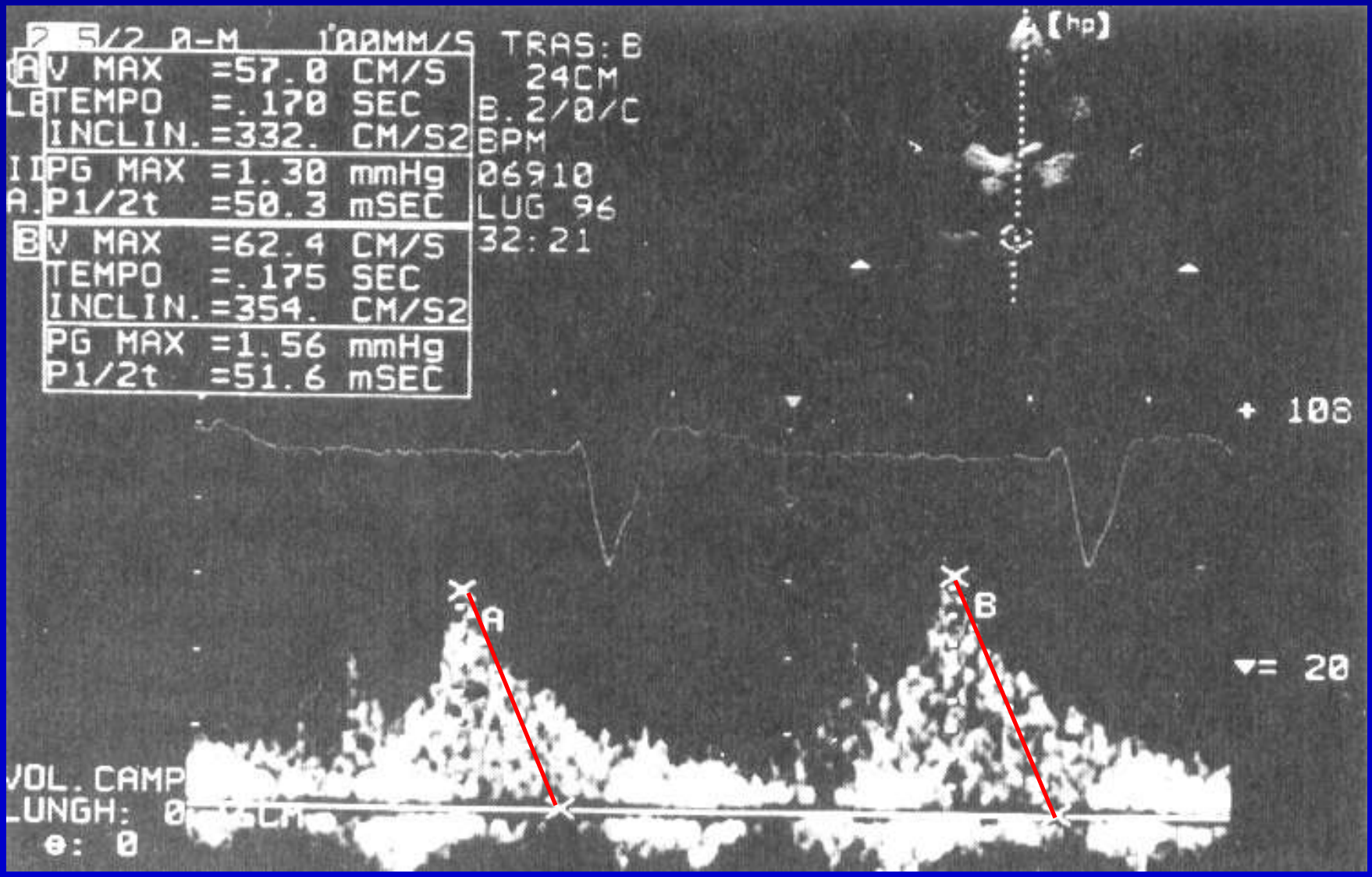


Chirillo F et al.
J Am Coll Cardiol 1997;30:19

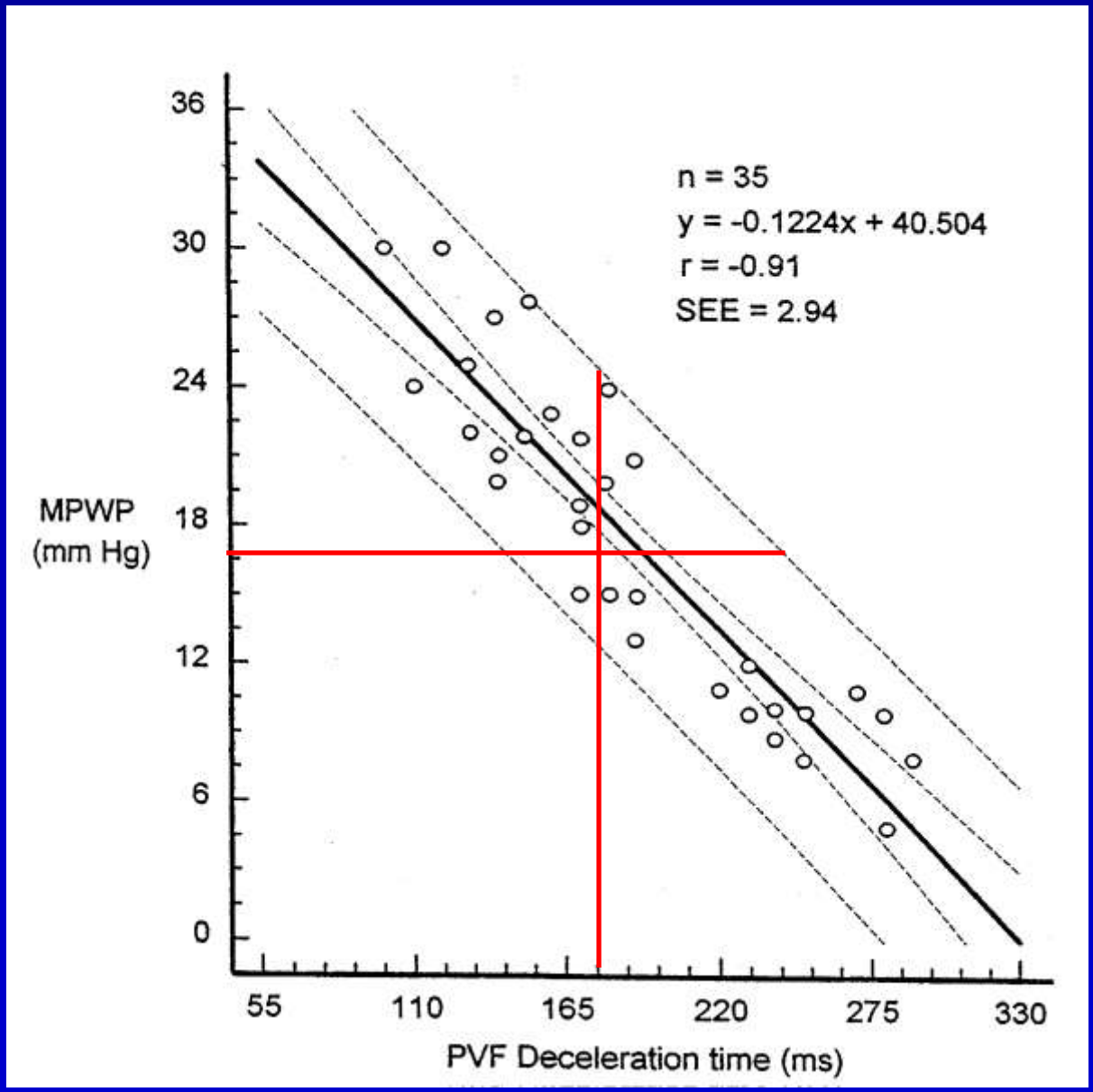
Pulmonary Venous Doppler and LV Diastolic Pressure



Pulmonary Venous Doppler and LV Diastolic Pressure



Pulmonary Venous Doppler and LV Diastolic Pressure



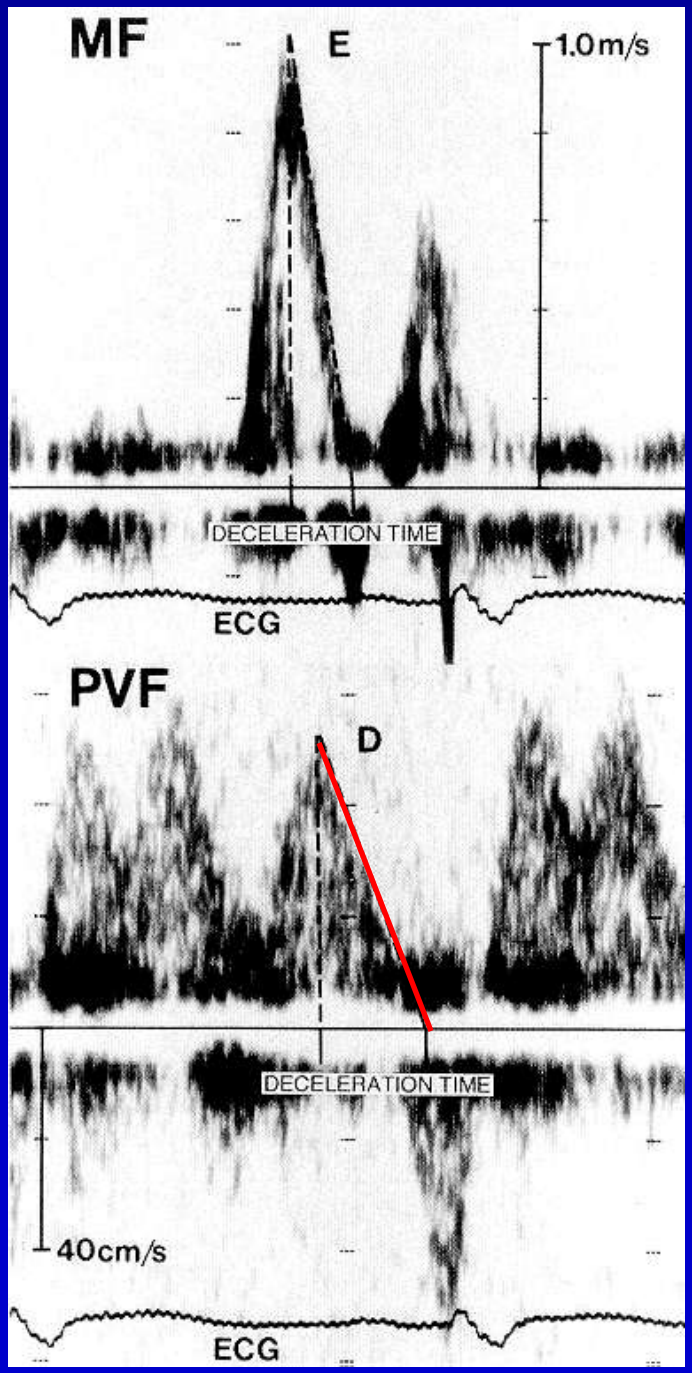
Chirillo F et al.
J Am Coll Cardiol
1997;30:19

Pulmonary Venous Doppler and Wedge Pressure

- 141 patients with acute first MI and sinus rhythm
- Time since MI 2.1 days, <7 da
- Exclusions: merging of LVIT E and A waves, valvular disease
- Simultaneous PCWP
- E deceleration – negative correlation with PCWP
- PV deceleration – strong negative correlation with PCWP

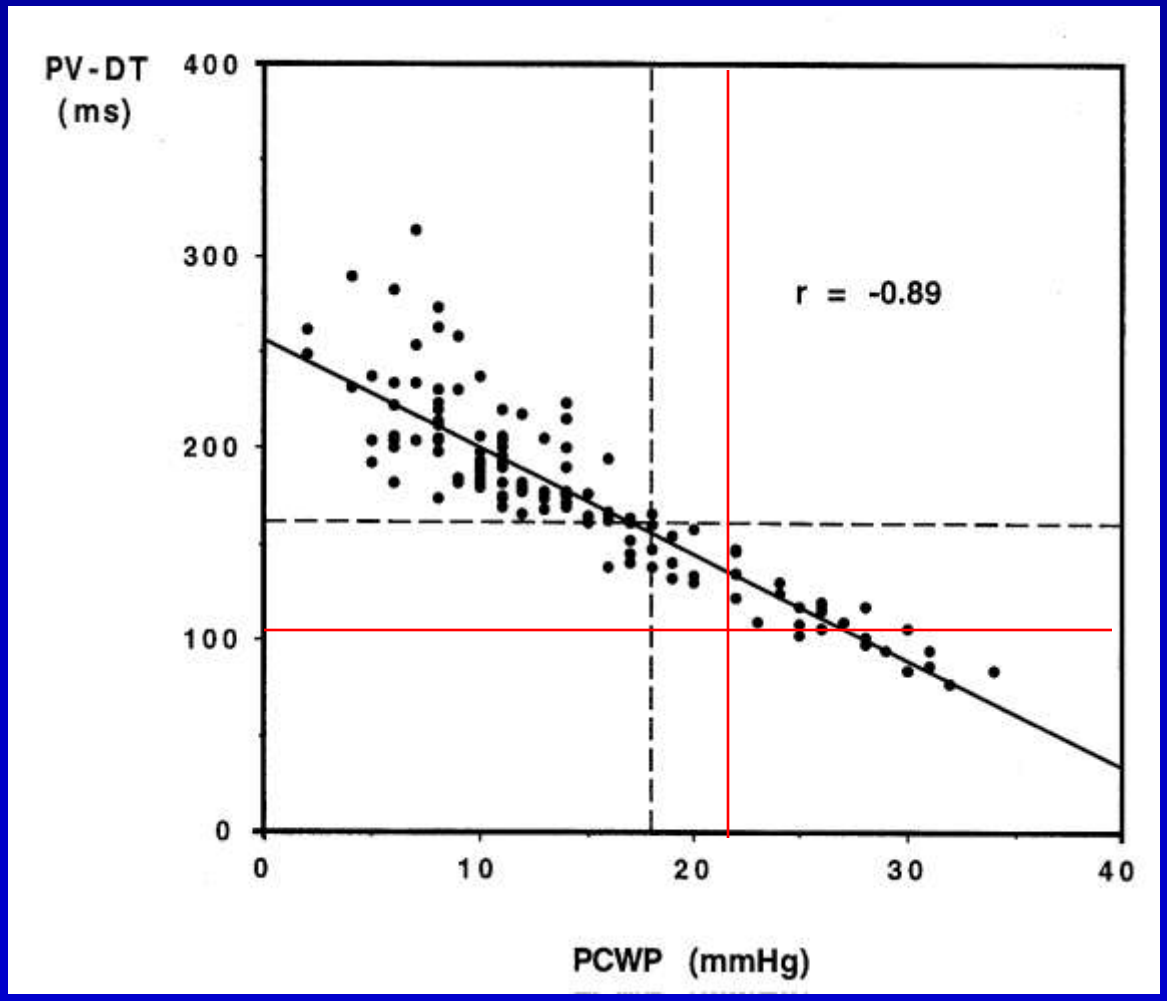
Yamamuro A et al. J Am Coll Cardiol 1999;34:90

Pulmonary Venous Doppler and Wedge Pressure



Yamamuro A et al.
J Am Coll Cardiol 1999;34:90

Pulmonary Venous Doppler and Wedge Pressure



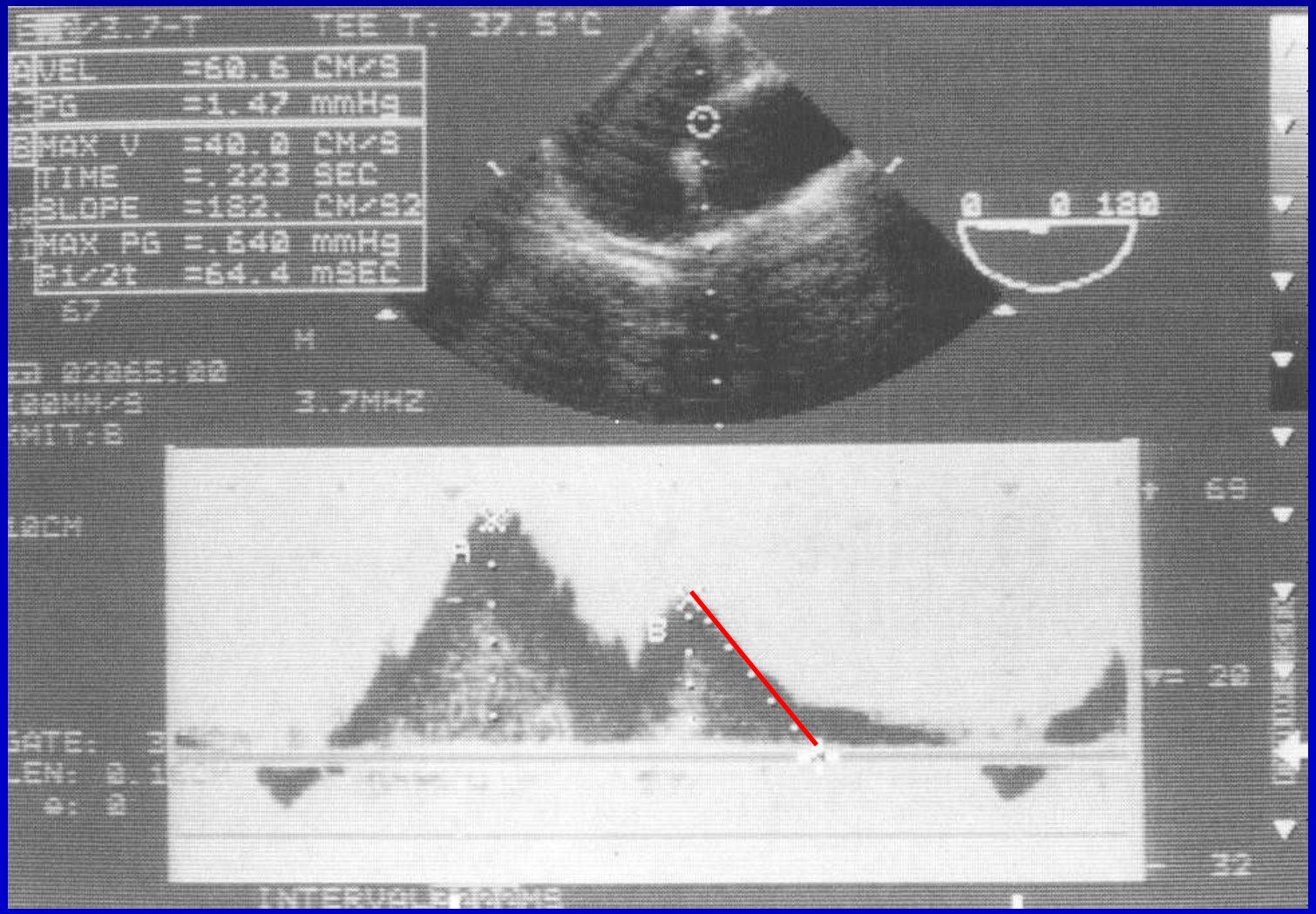
Yamamuro A et al. J Am Coll Cardiol 1999;34:90

Pulmonary Venous Doppler and LV Diastolic Pressure

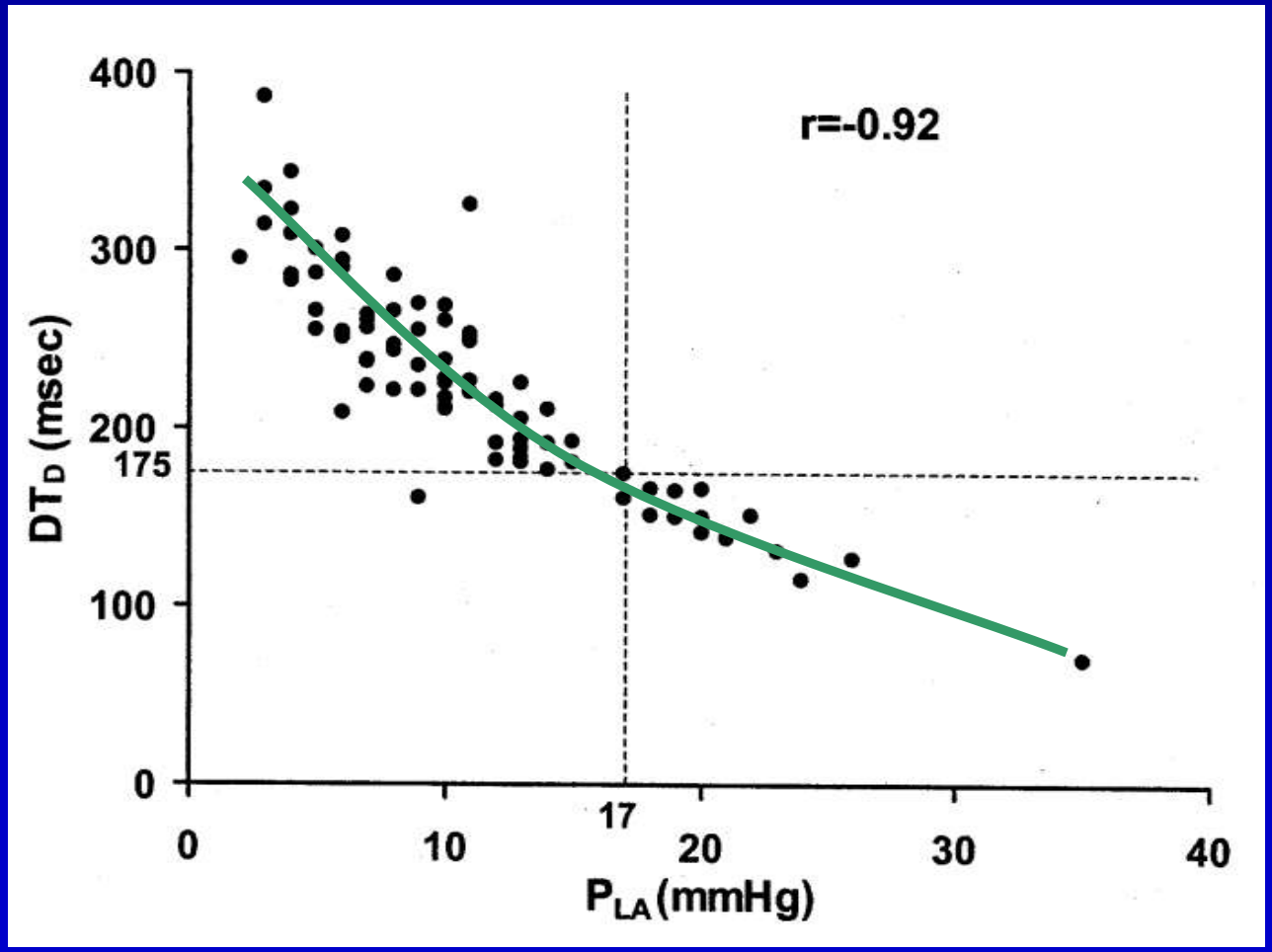
- 93 patients undergoing surgery (CABG or AVR), intraoperative TEE, S-G cath and LA cath
- End-expiration (positive pressure)
- PV Doppler 10 mm from orifice of a superior pulmonary vein
- If PV-D deceleration was bimodal, the first and steeper portion was extrapolated to zero to obtain deceleration time (DT_D)
- DT_D<175 msec implies LA pressure >17 mmHg

Kinnaird TD et al. J Am Coll Cardiol 2001;37:2025

Pulmonary Venous Doppler and LA Pressure



Pulmonary Venous Doppler and LV Diastolic Pressure



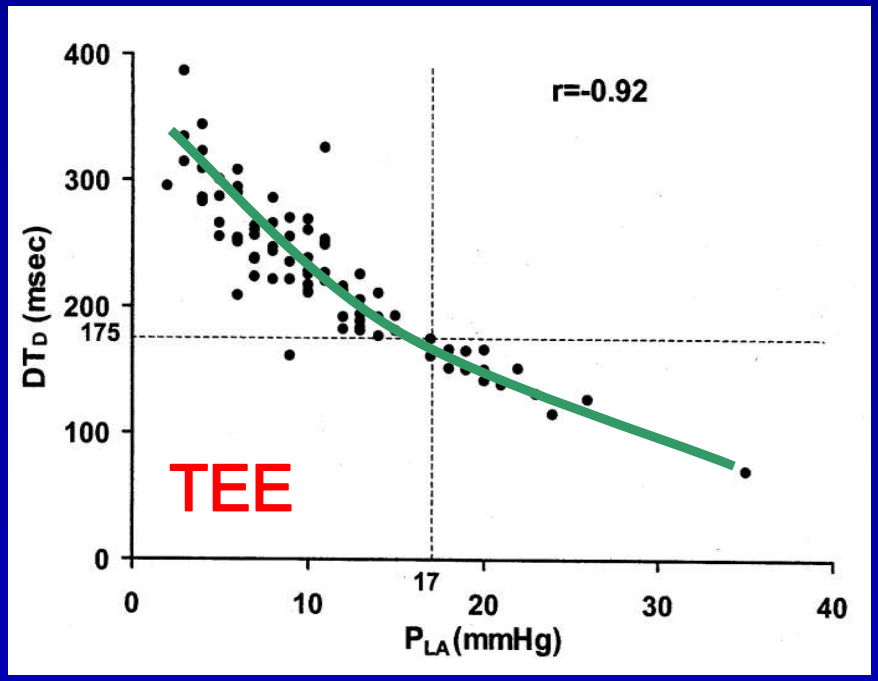
Bland-Altman plot variation up to 6 mmHg

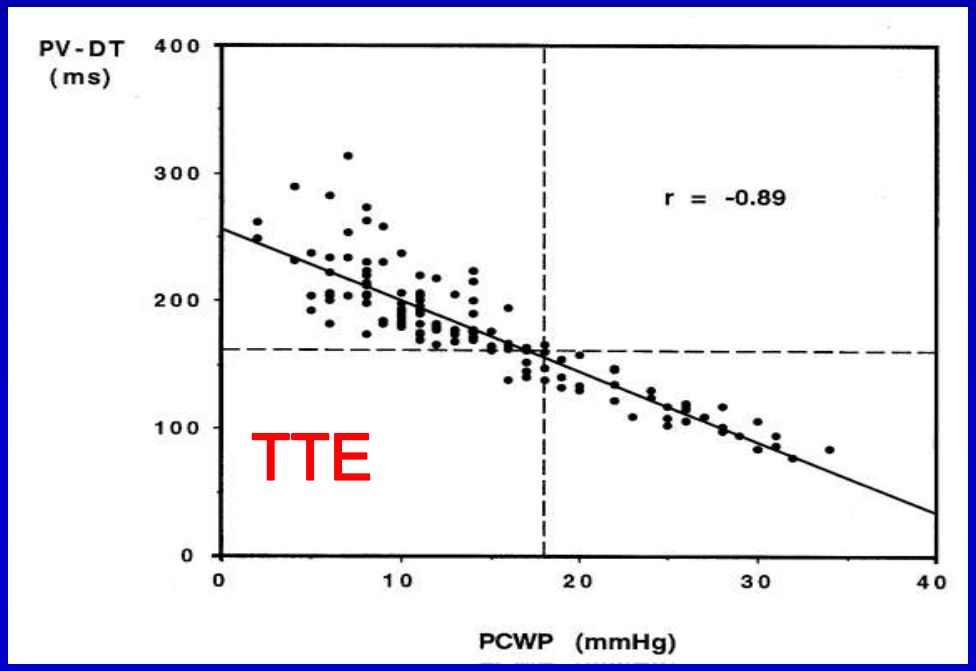
Similar results in 2 other studies, one in atrial fibrillation and one in recent MI

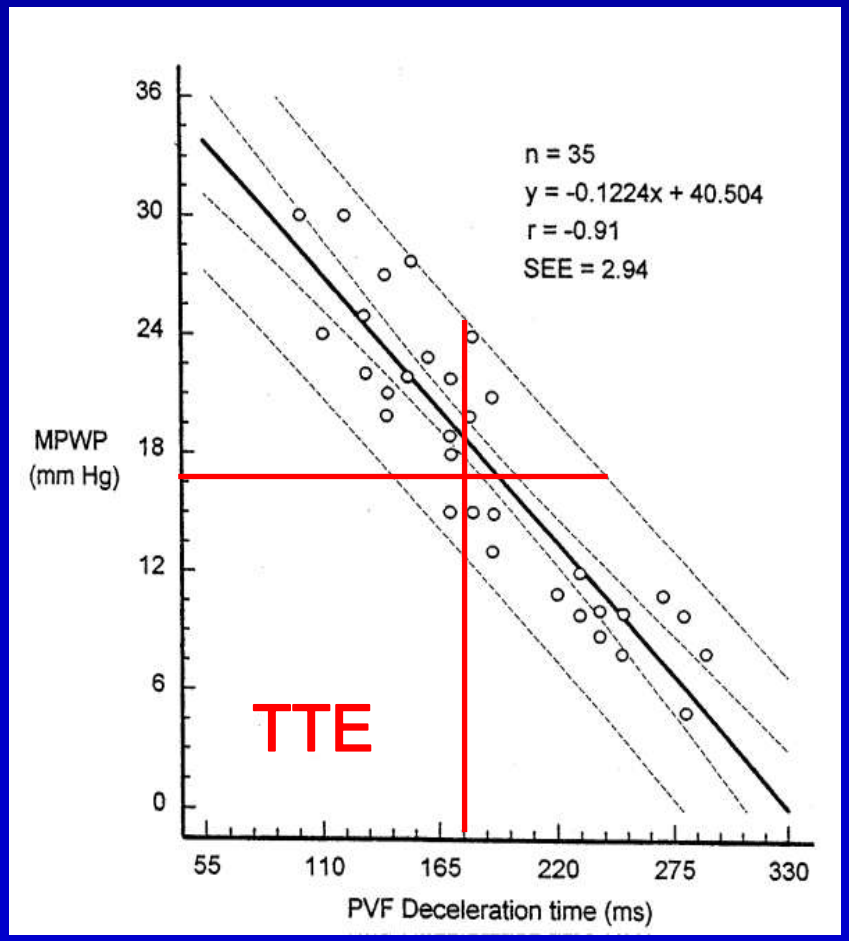
Kinnaird TD et al. J Am Coll Cardiol 2001;37:2025

PV Deceleration and LA Pressure

Abscissa and Ordinate Inverted

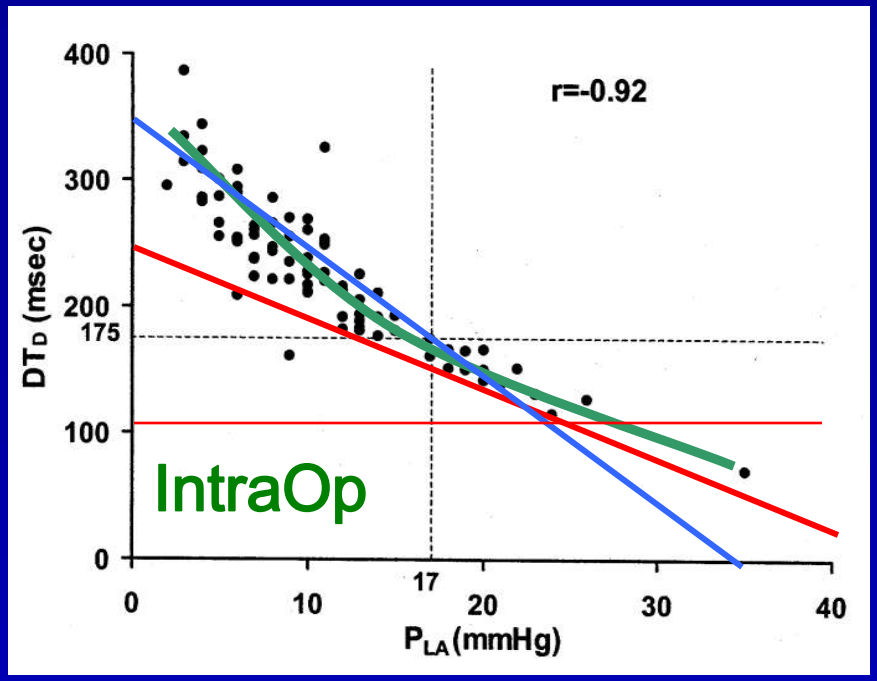


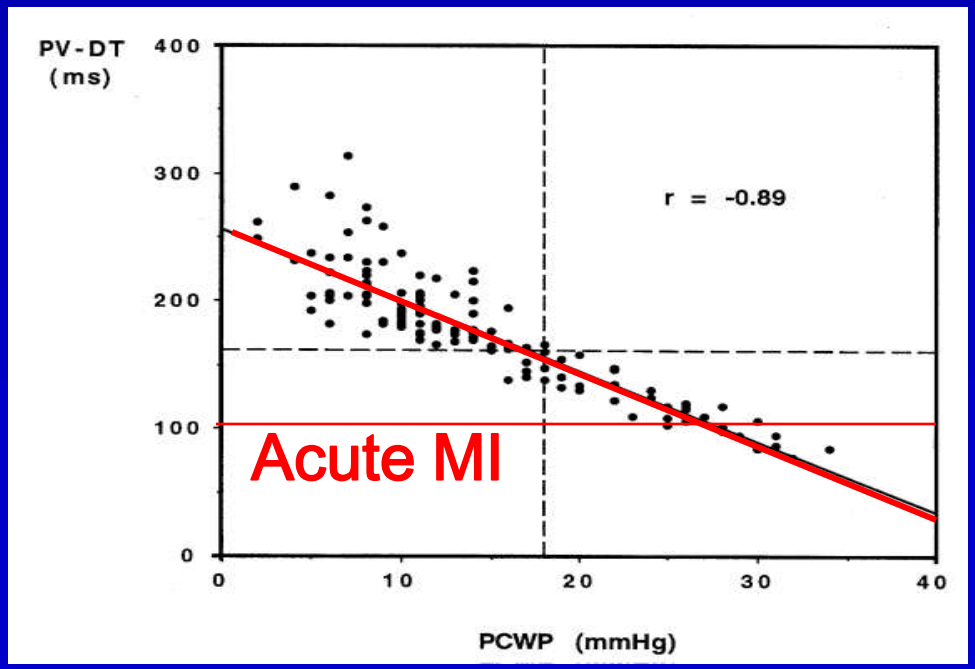


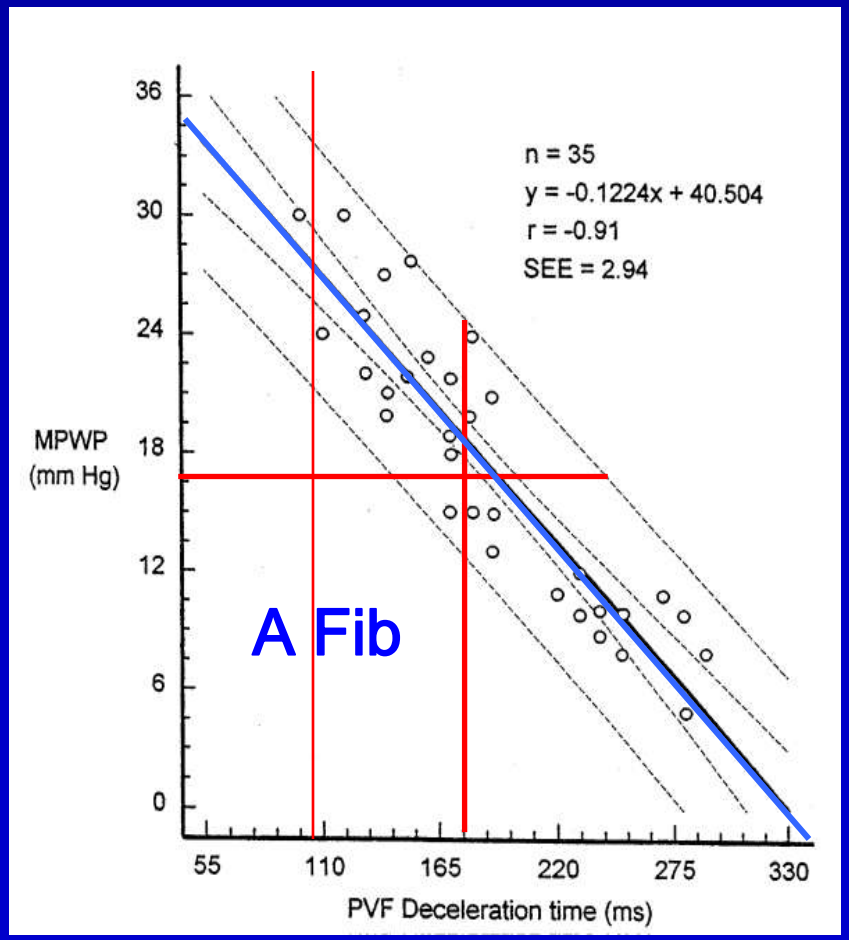


PV Deceleration and LA Pressure

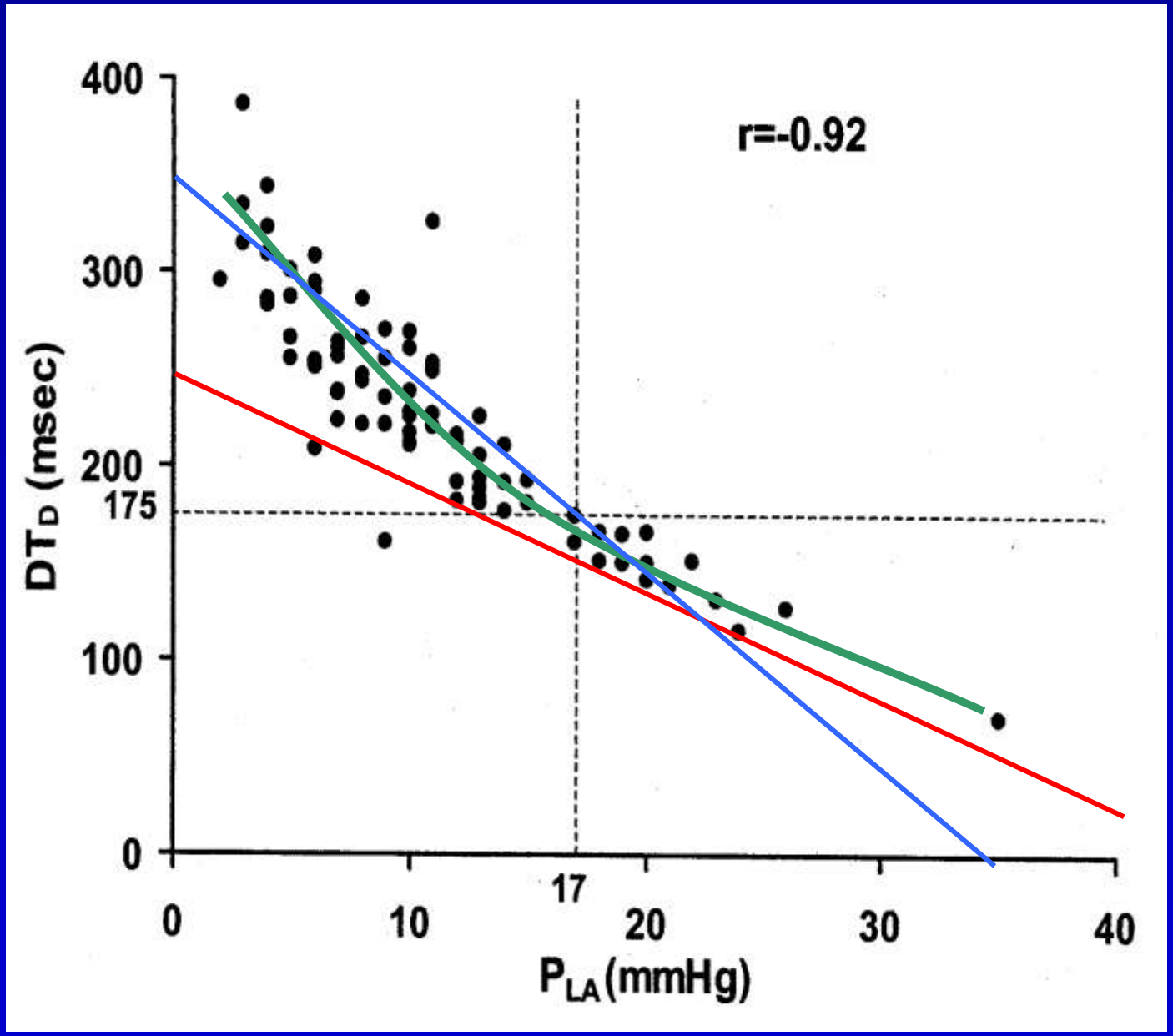
Abscissa and Ordinate Inverted



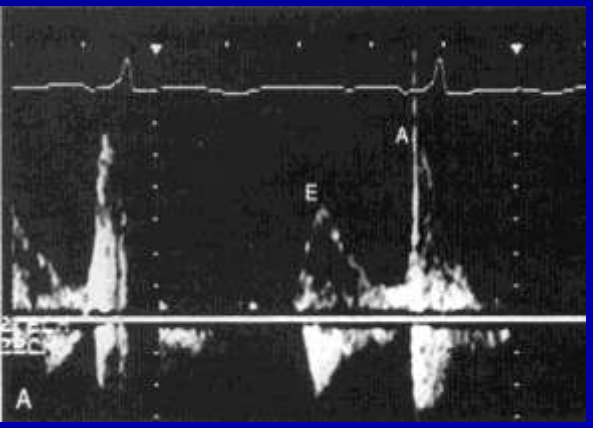




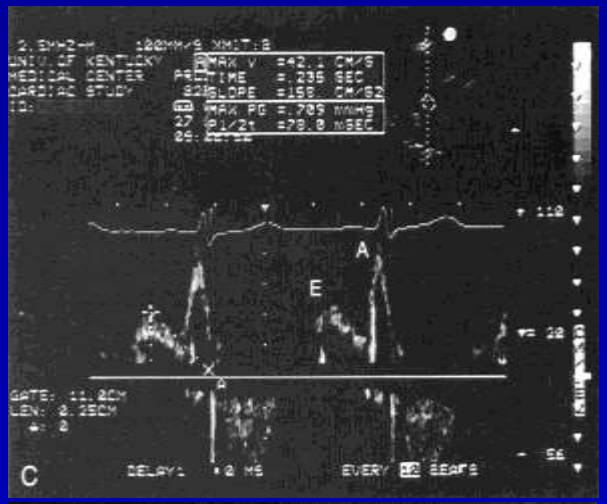
PV Deceleration and LA Pressure

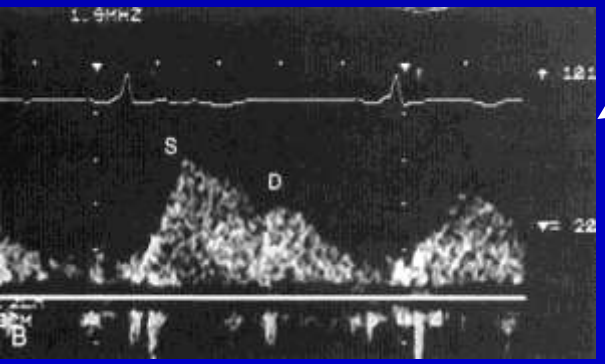


Impaired LV Relaxation

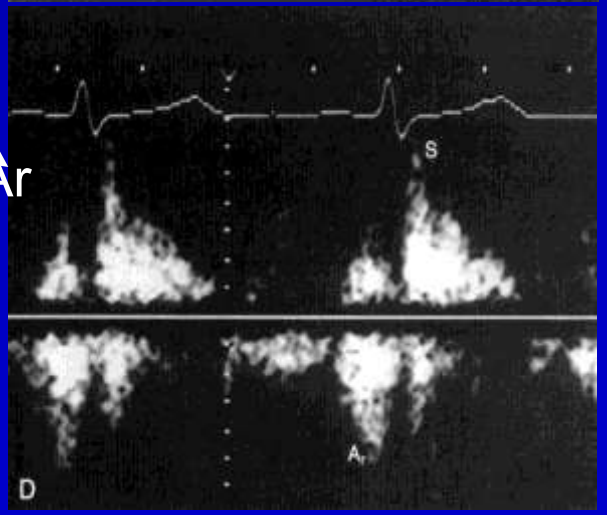


Transmitral flow:
Small E, slow E decel,
Large A





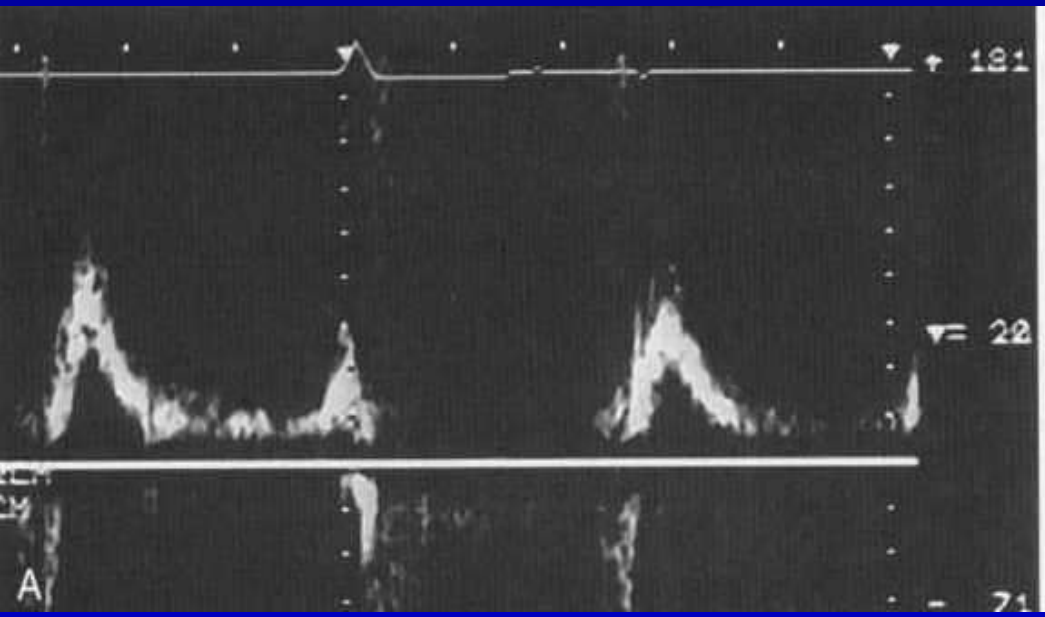
Pulmonary venous flow:
smaller D wave,
larger S wave, variable Ar

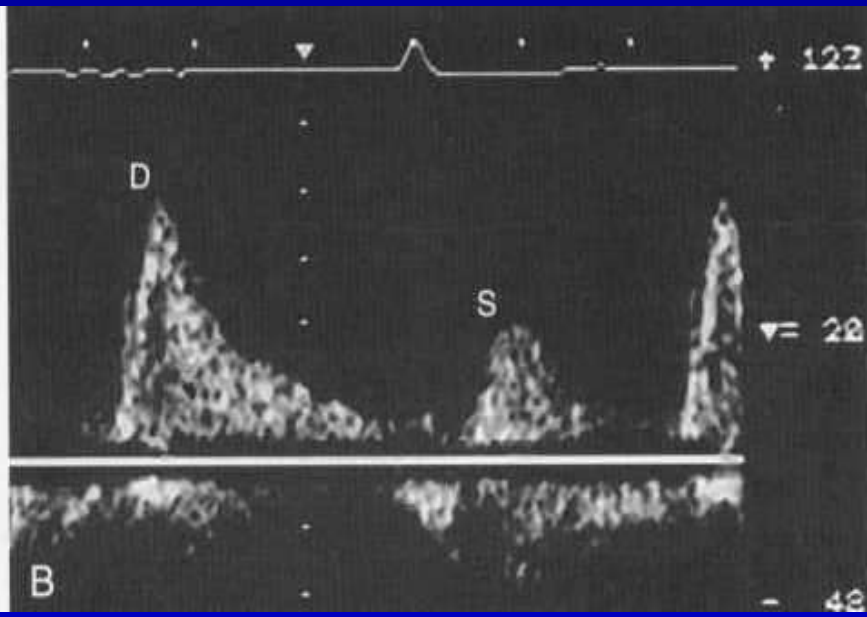


2 hypertensive patients with impaired relaxation

Smith, Mikel, in Otto, 1997

Pseudonormal Diastolic Pattern



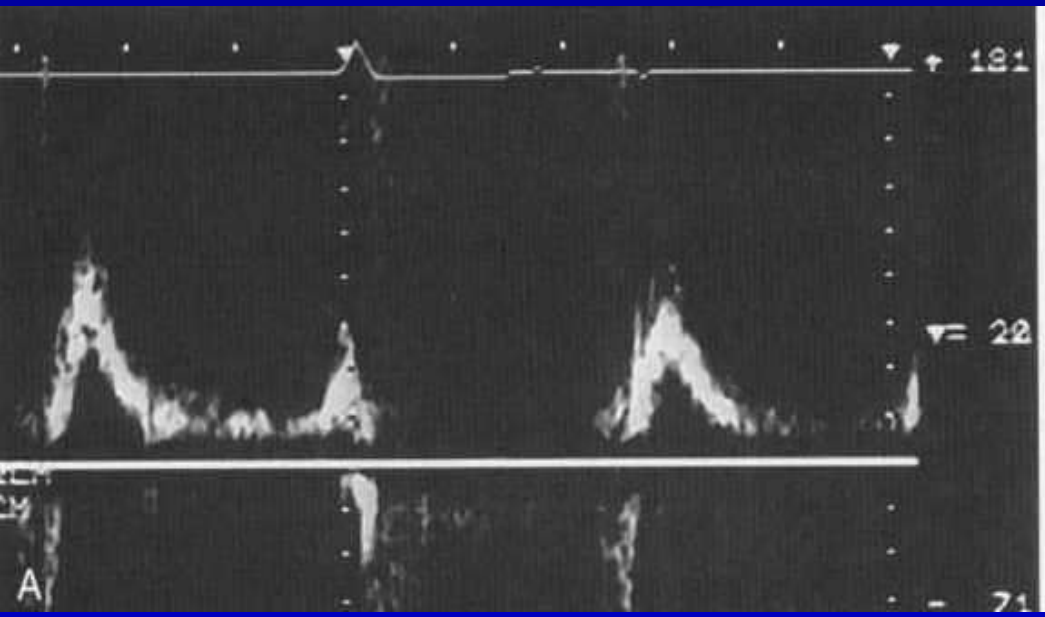


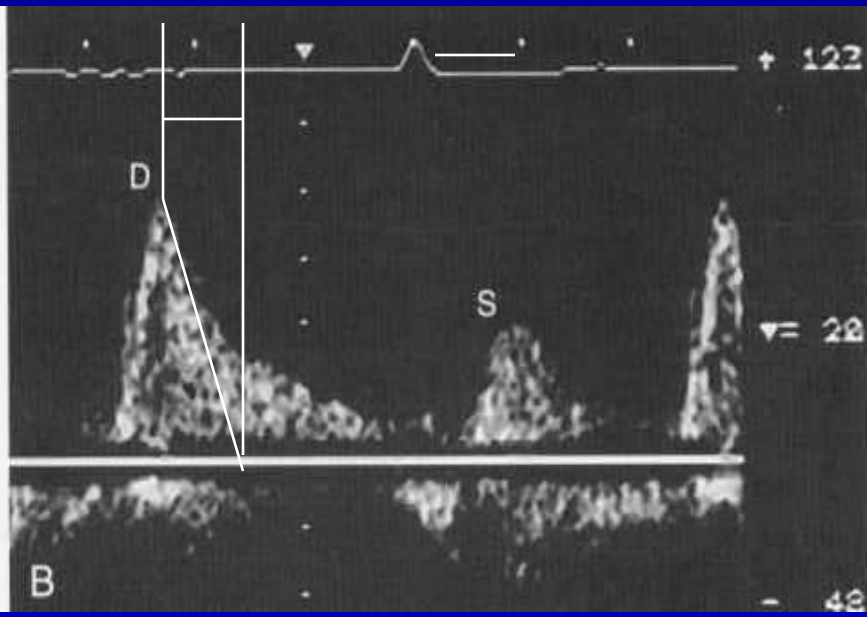
Transmitral flow: Normal E and A pattern

Pulmonary vein flow: reduced S wave from decreased atrial relaxation, possibly large Ar wave from reduced ventricular compliance

Smith, Mikel, in Otto, 1997

Pseudonormal Diastolic Pattern



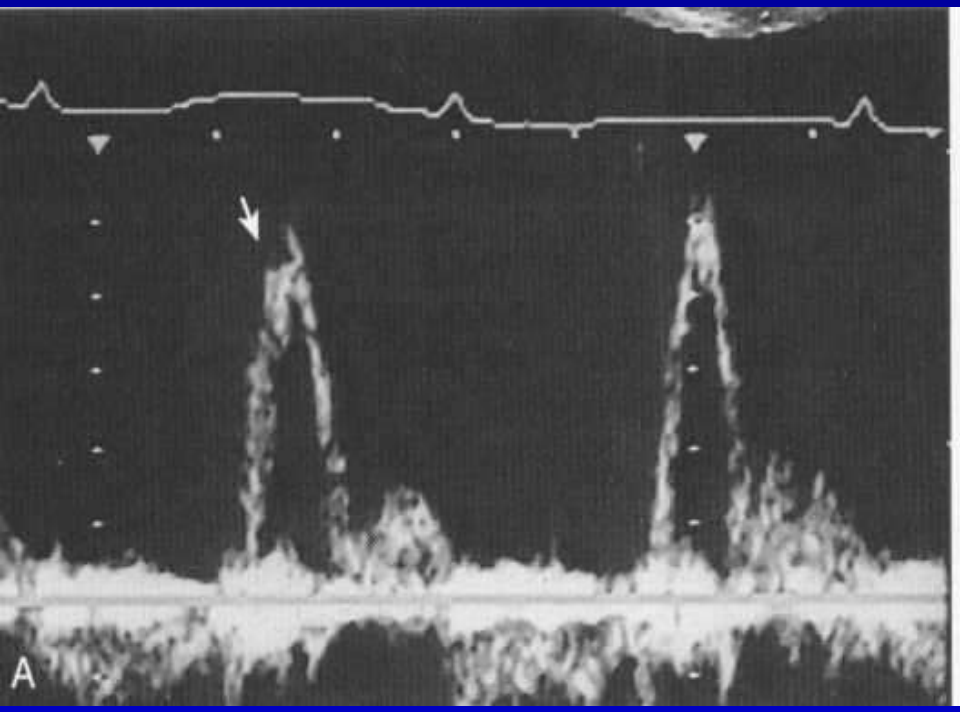


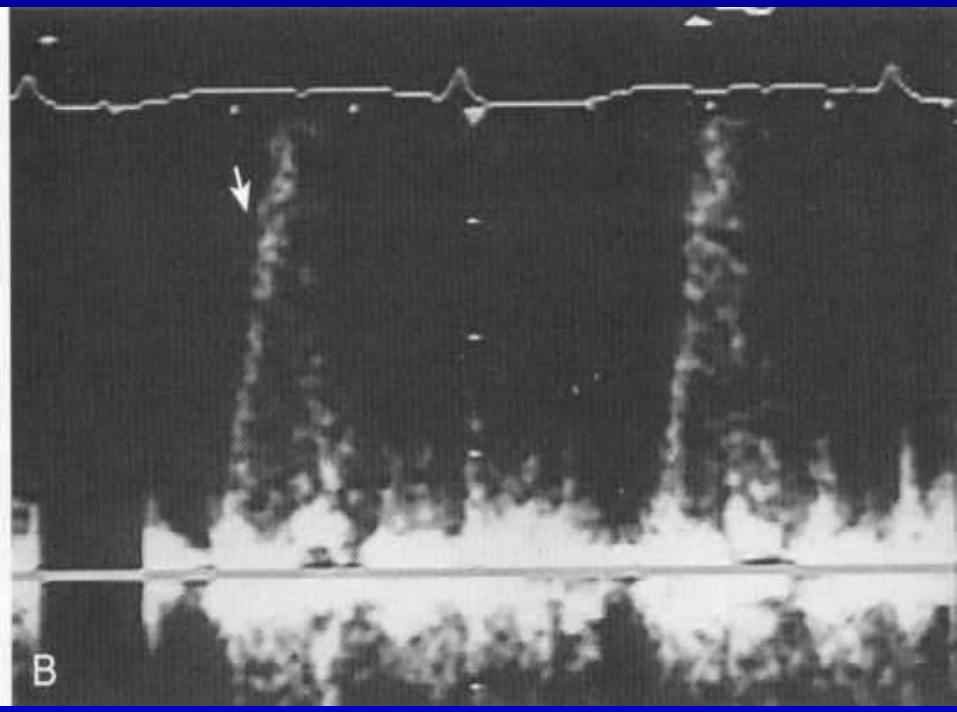
Transmitral flow: Normal E and A pattern

Pulmonary vein flow: reduced S wave from decreased atrial relaxation, possibly large Ar wave from reduced ventricular compliance

Smith, Mikel, in Otto, 1997

Restrictive Diastolic Pattern



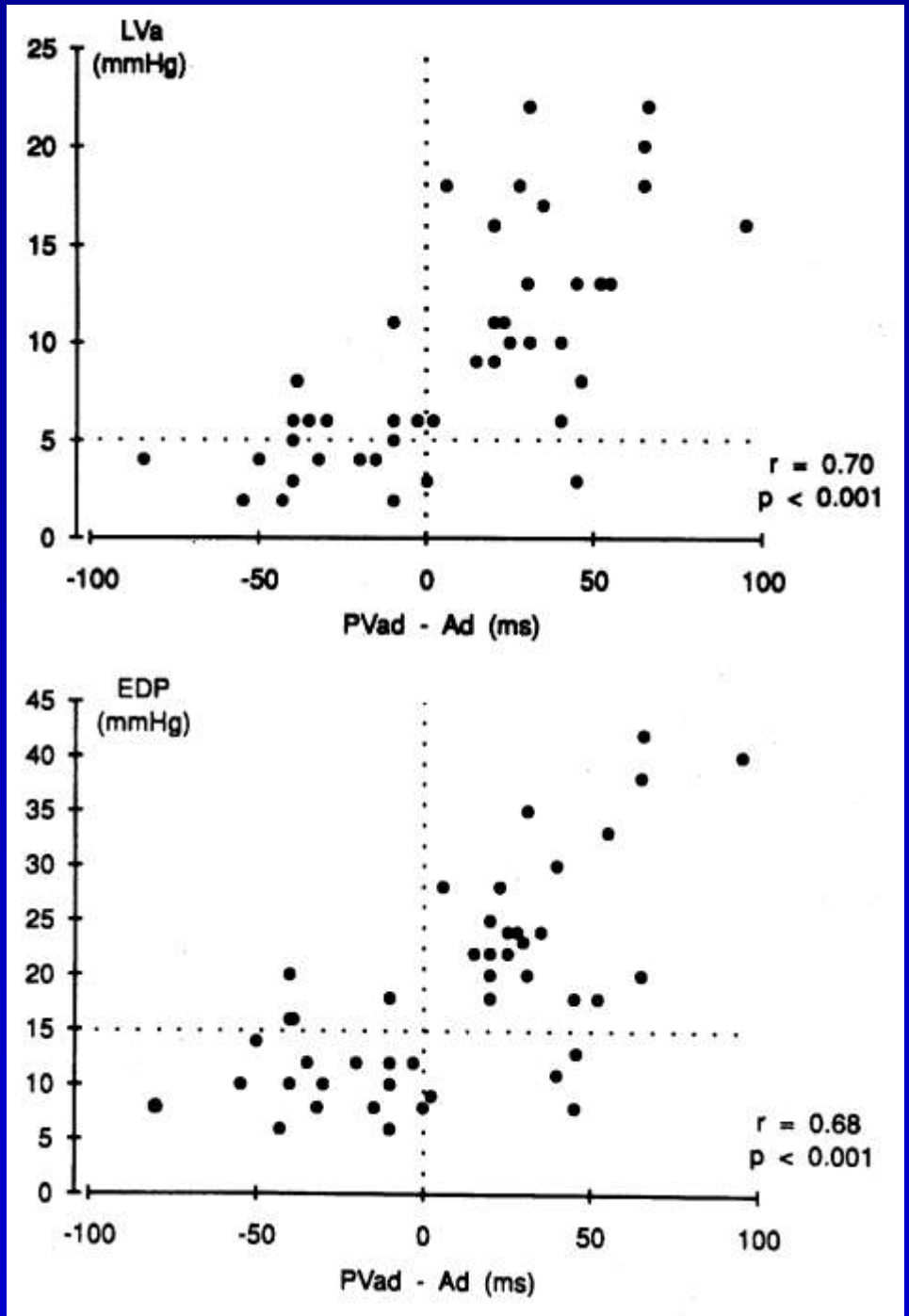


Transmitral flow
restrictive pattern
large E, short decel time, small A

Pulmonary vein flow
small S wave, large D wave,
rapid D descent, no Ar (atrial failure)

Smith, Mikel, in Otto, 1997

Assessing LVIT and PV flows: Comparing LVIT-A with PV-Ar

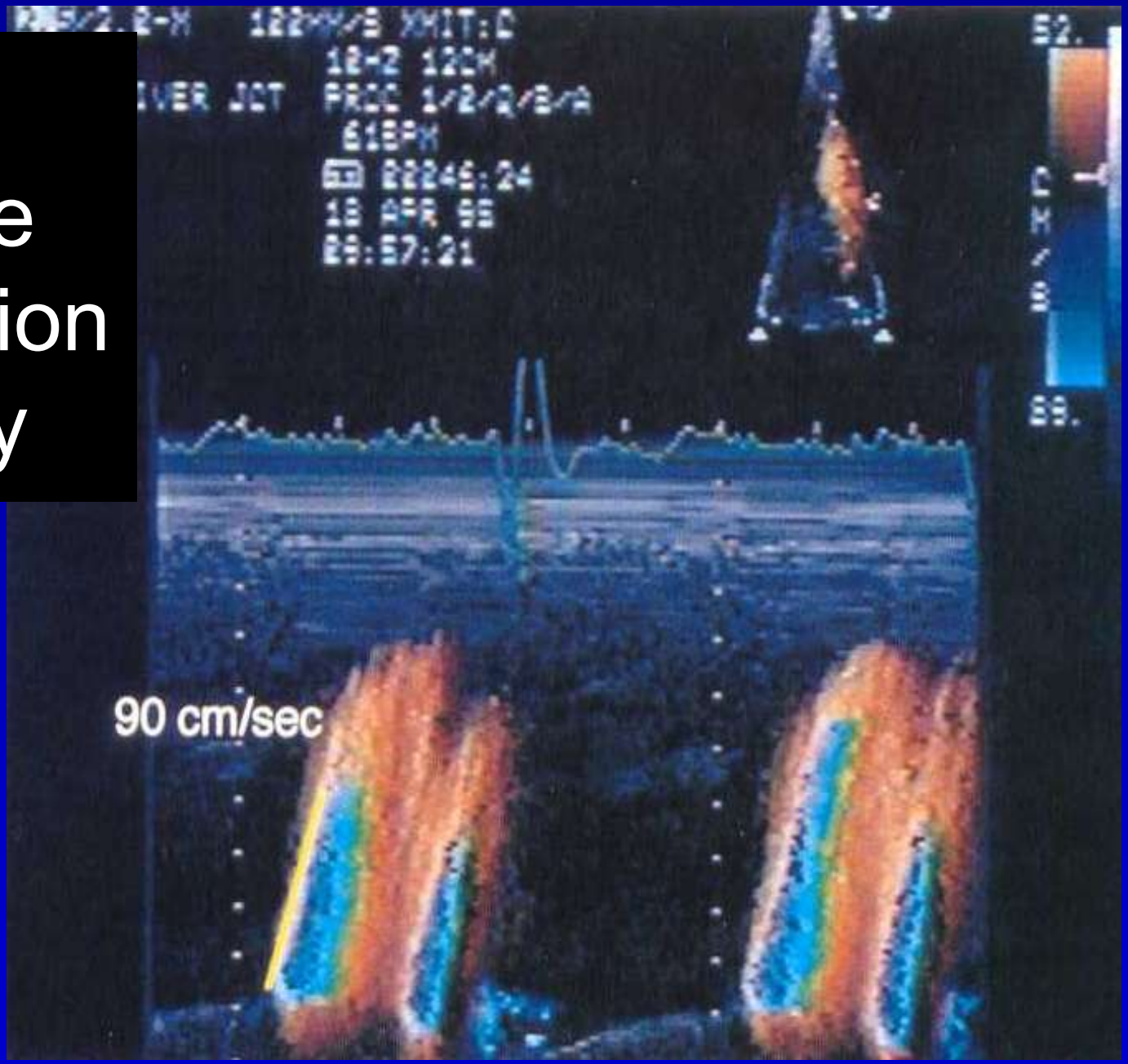


Rossvoll O et al.
J Am Coll Cardiol
1993;21:1687

Doppler Assessment of Diastole

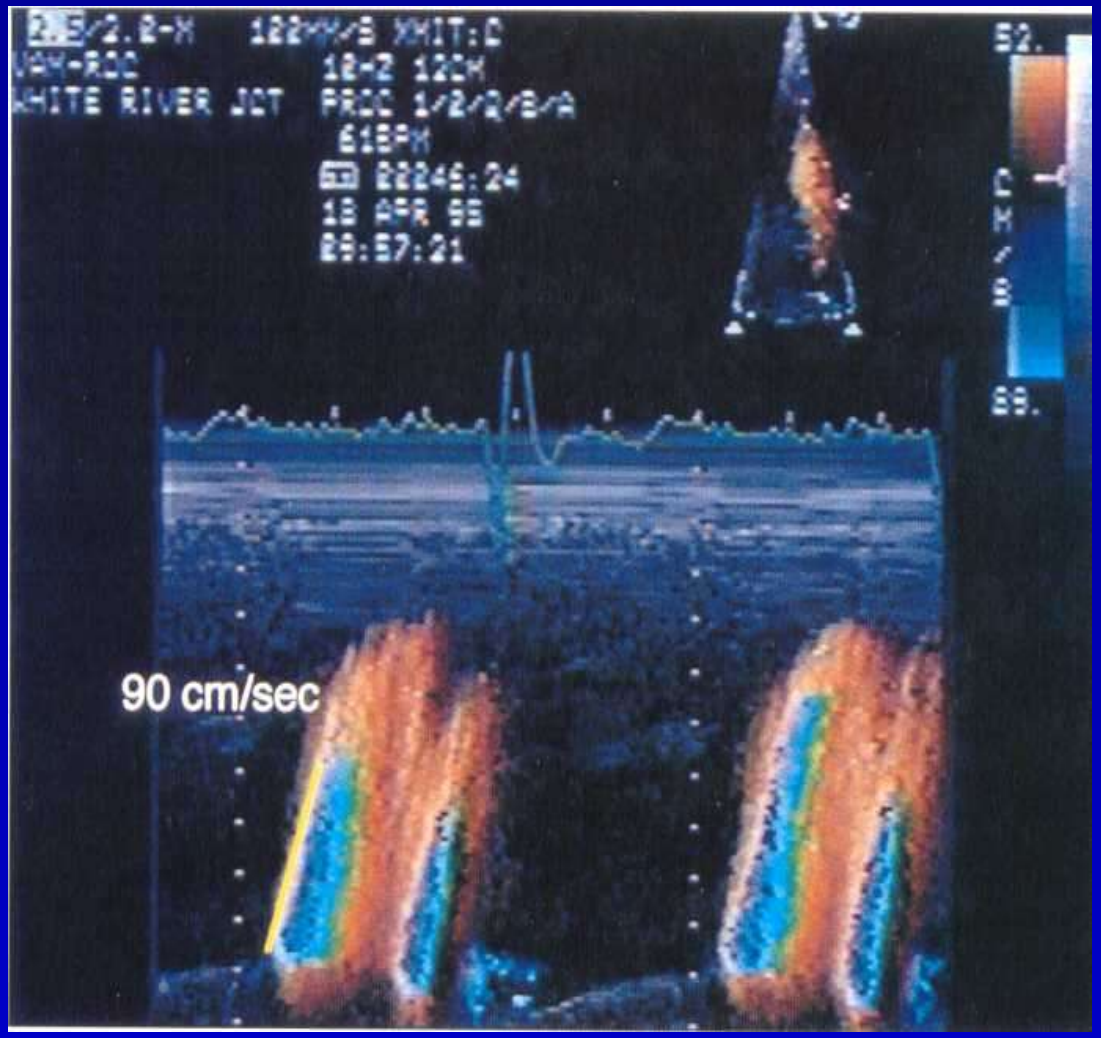
- Transmitral flow assessment
- Isovolumic relaxation time
- Pulmonary venous flow assessment
- **Flow propagation velocity**
- Pulse transit time
- Tissue Doppler imaging

Color M-Mode Propagation Velocity



Garcia et al JASE 1999; 12:129

Color M-Mode Propagation Velocity

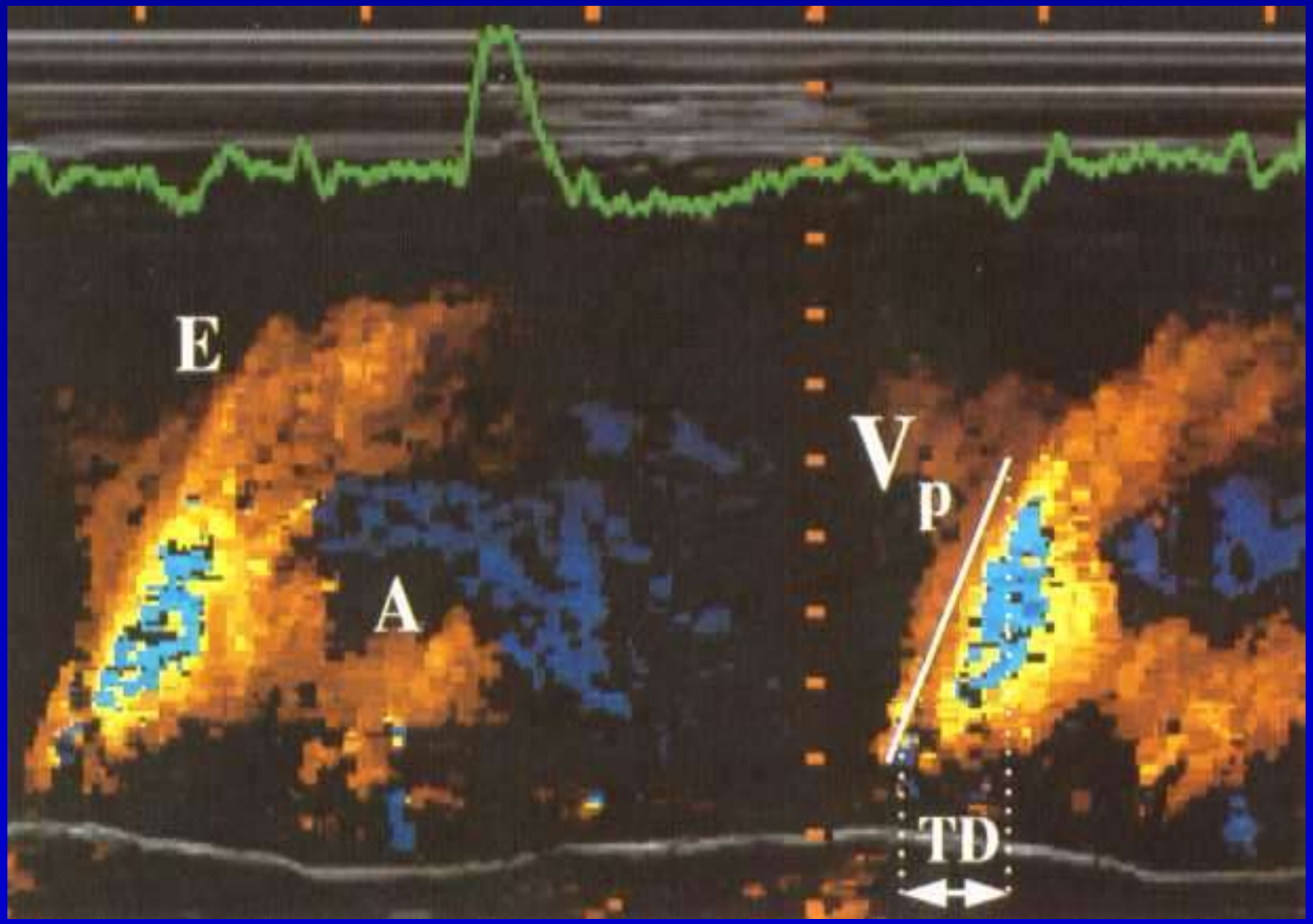


Measure slope:

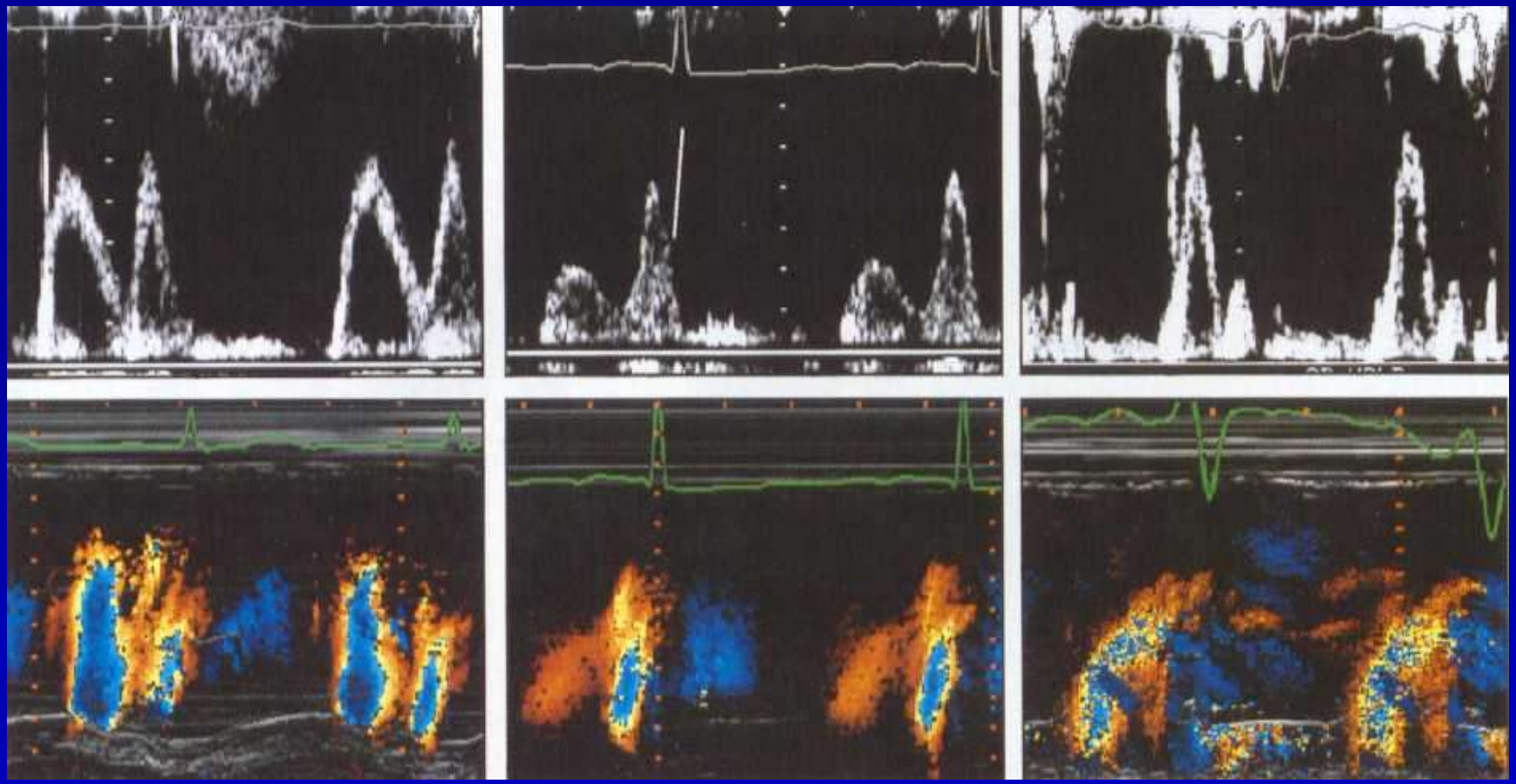
- First aliasing velocity
- Begin at mitral tips
- to 4 cm distally
- May be curvilinear
- End-expiration
- Average several measures
- Adjust scale or baseline to produce aliasing (50-75% of peak E transmural PW Doppler)

Garcia, JACC 1998; 32:865

Color M-Mode Propagation Velocity



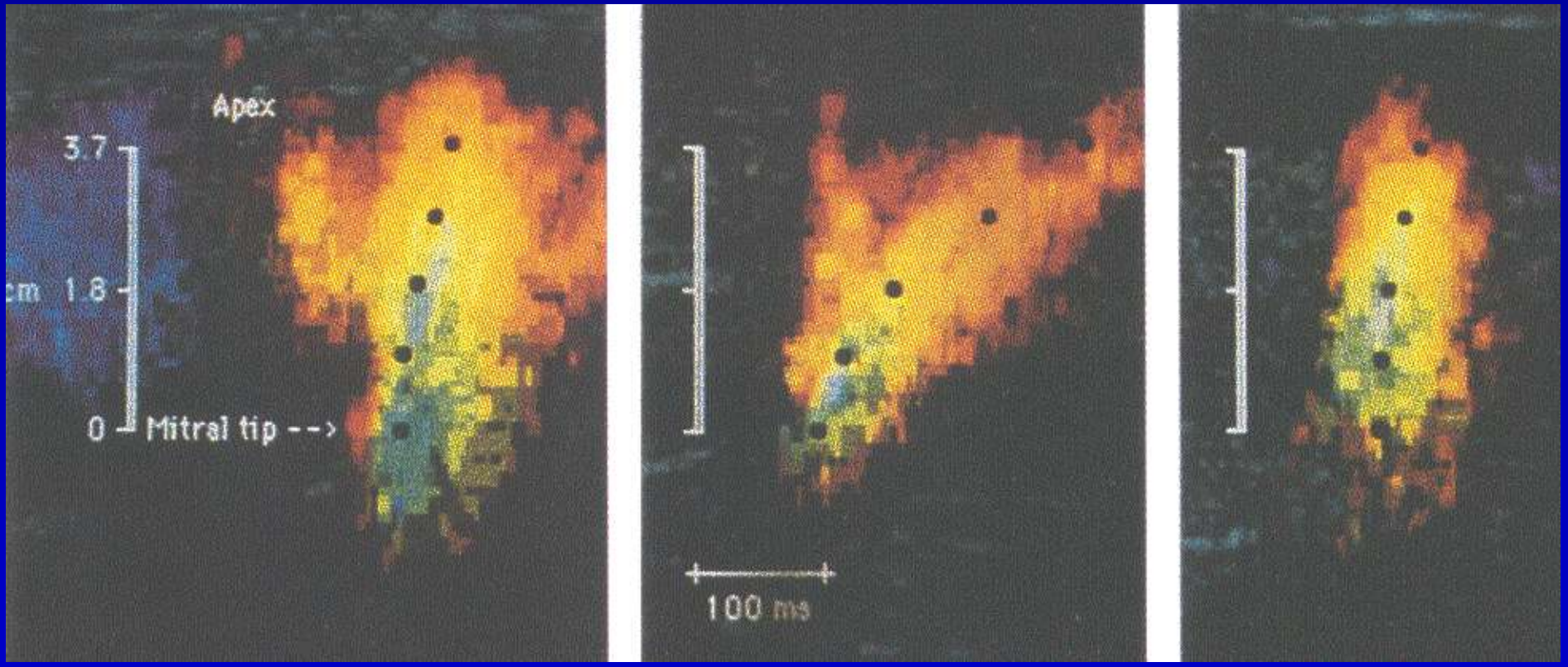
Garcia, JACC 1998; 32:865



Normal	Delayed Relaxation	Restrictive
LVIT-E normal Vp normal	LVIT-E reduced Vp reduced	LVIT-E augmented Vp reduced

Garcia, JACC 1998; 32:865

Color Flow Propagation Velocity



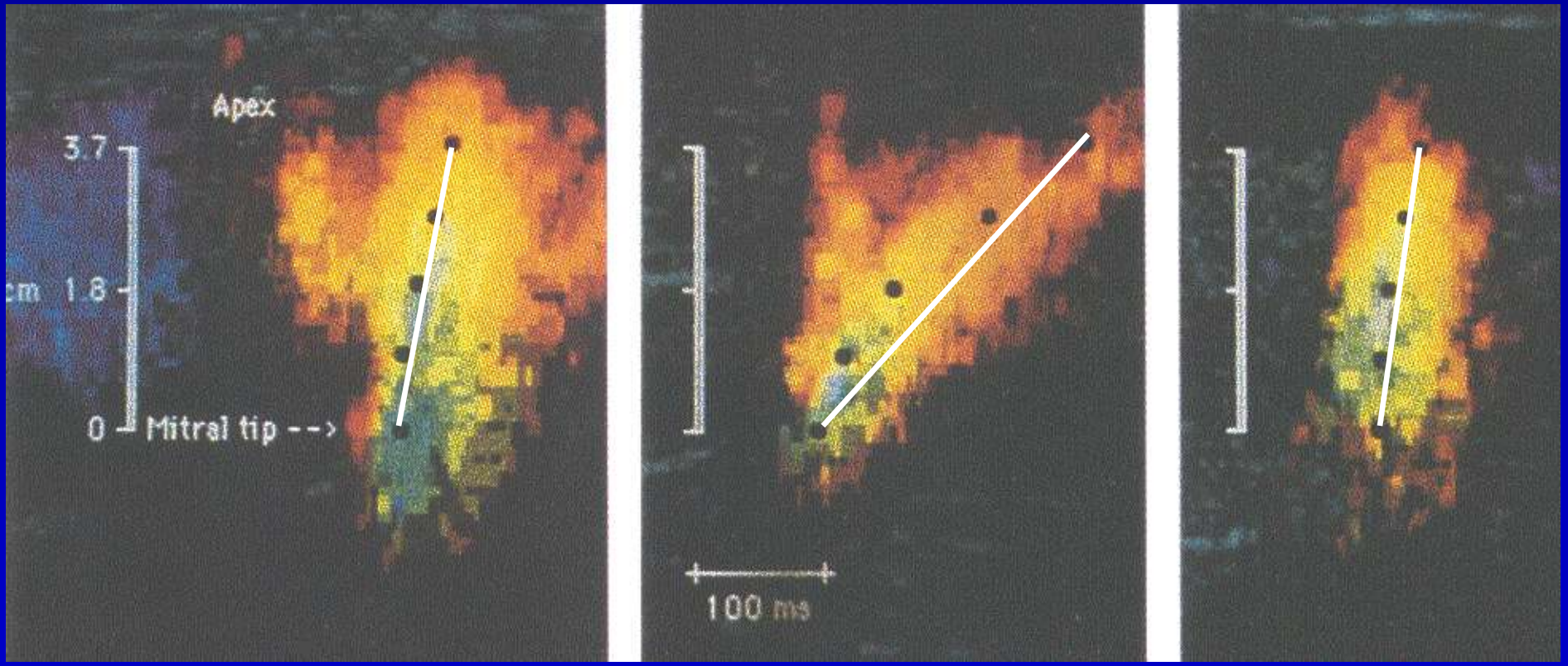
Resting
Normal

LAD balloon occlusion
Delay filling

Balloon down
Normal

Stugaard M. Circulation 1993;88:2708

Color Flow Propagation Velocity



Resting
Normal

LAD balloon occlusion
Delay filling

Balloon down
Normal

Stugaard M. Circulation 1993;88:2708

Prognostic Value of LVIT Pattern and Flow Propagation Velocity

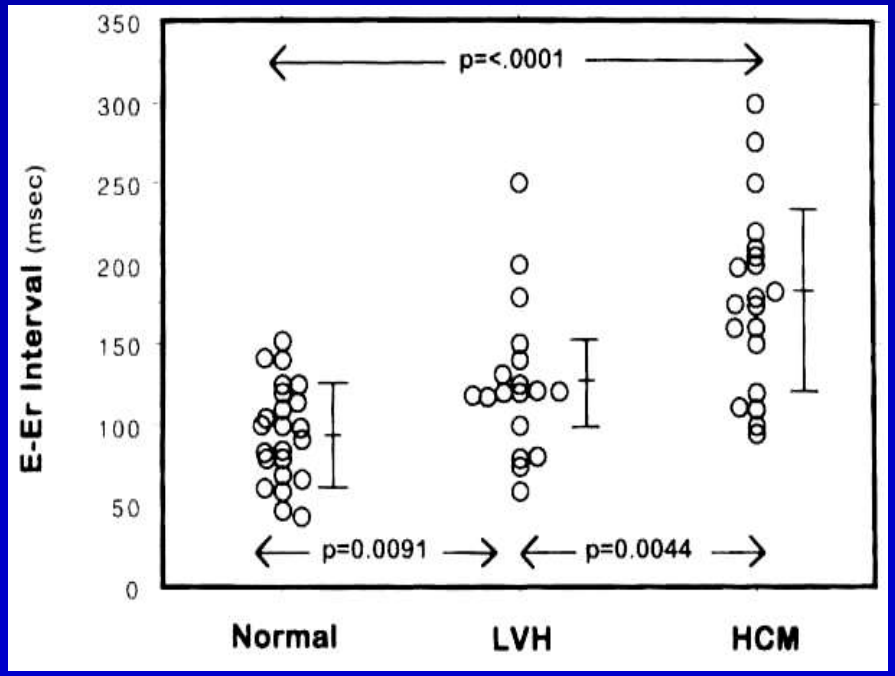
- 125 pts with first MI
  - If DT>140 and <240ms and VP>45 cm/s = normal (38 pts)
  - DT>240 = impaired relaxation (38 pts)
  - DT nl and VP<45 cm/s = pseudonormal (26 pts)
  - DT<140 = restrictive (23 pts)
- Progressive higher age, admission HR, peak CK, Killip class, and lower BP
- Progressive larger ventricles, lower EF, worse wall motion score, shorter IVRT, and MR regurgitation
- Restrictive or pseudonormal filling pattern was risk for death, relative risk 4 to 6, more than Killip class, age, wall motion, or peak CK

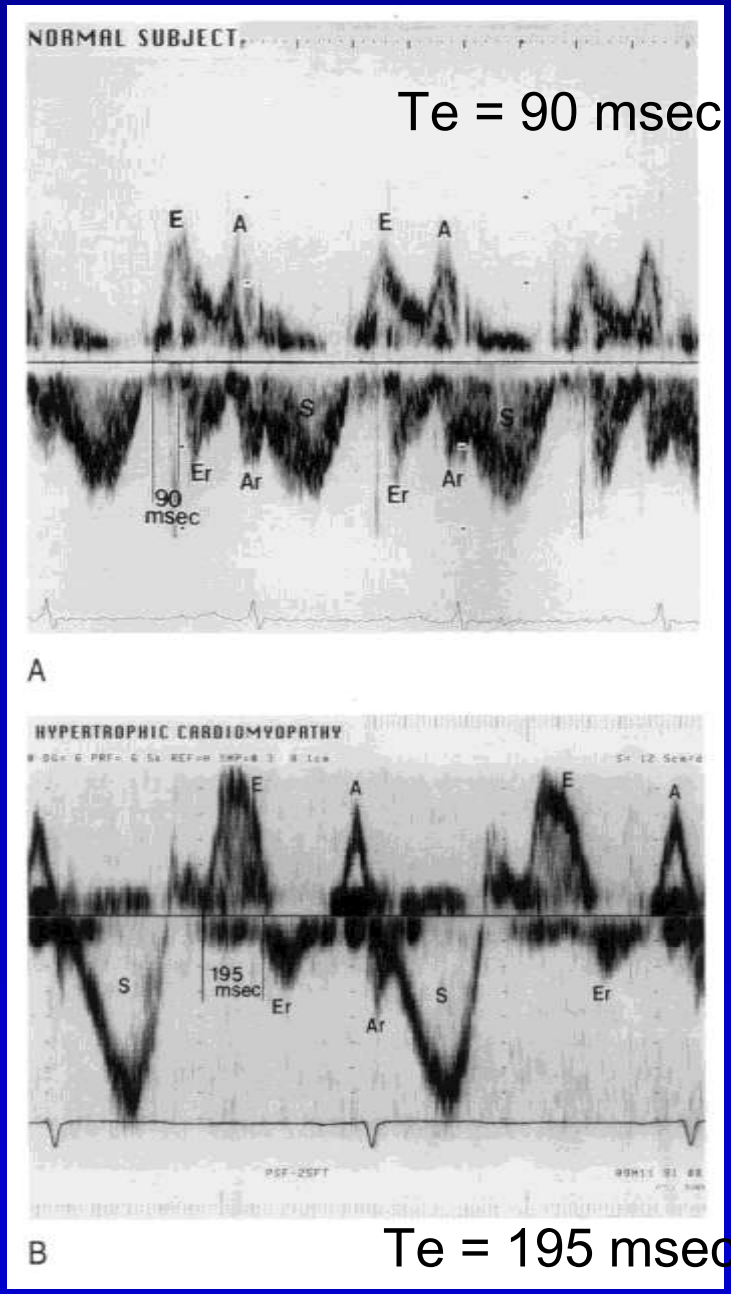
Moller JE et al. J Am Coll Cardiol 2000;36:1841

Doppler Assessment of Diastole

- Transmitral flow assessment
- Isovolumic relaxation time
- Pulmonary venous flow assessment
- Flow propagation velocity
- **Pulse transit time**
- Tissue Doppler imaging

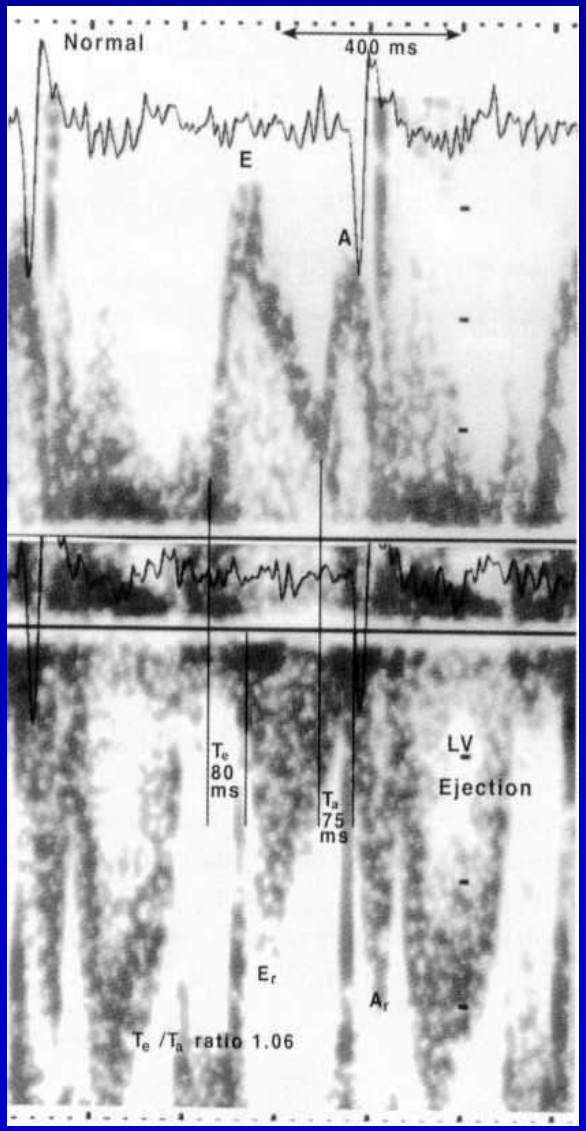
LV transit time in Early Diastole in Normal and Hypertrophic Cardiomyopathy



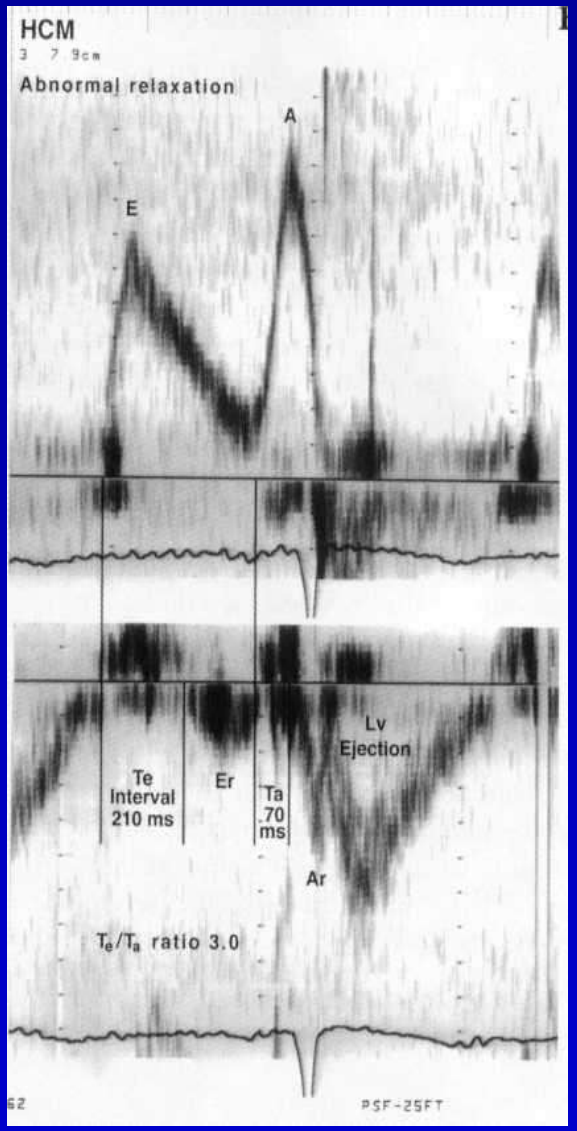


Pai, R, JASE 1999; 10:532

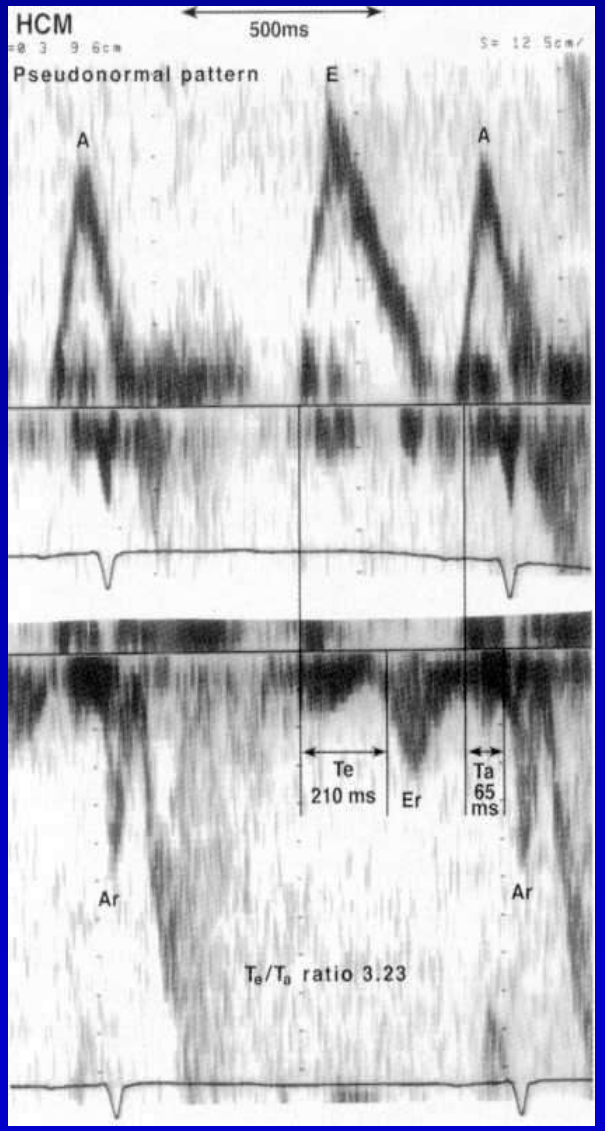
Transit time from LVIT to LVOT During early and late diastole



Te/Ta = 1.05



Te/Ta = 3.0



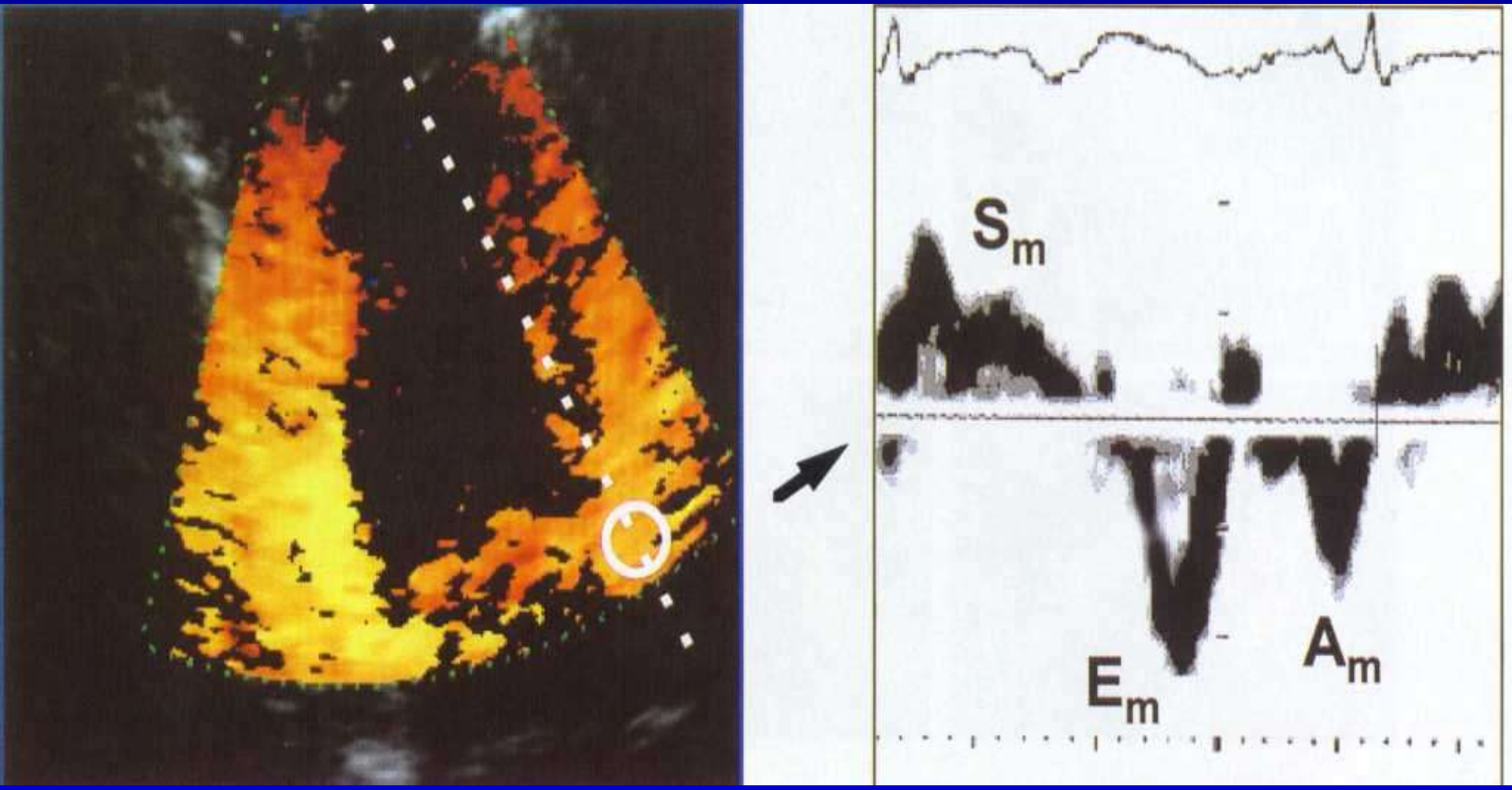
Te/Ta = 3.23

Pai, R et al, JASE 1999; 12:811

Doppler Assessment of Diastole

- Transmitral flow assessment
- Isovolumic relaxation time
- Pulmonary venous flow assessment
- Flow propagation velocity
- Pulse transit time
- **Tissue Doppler imaging**

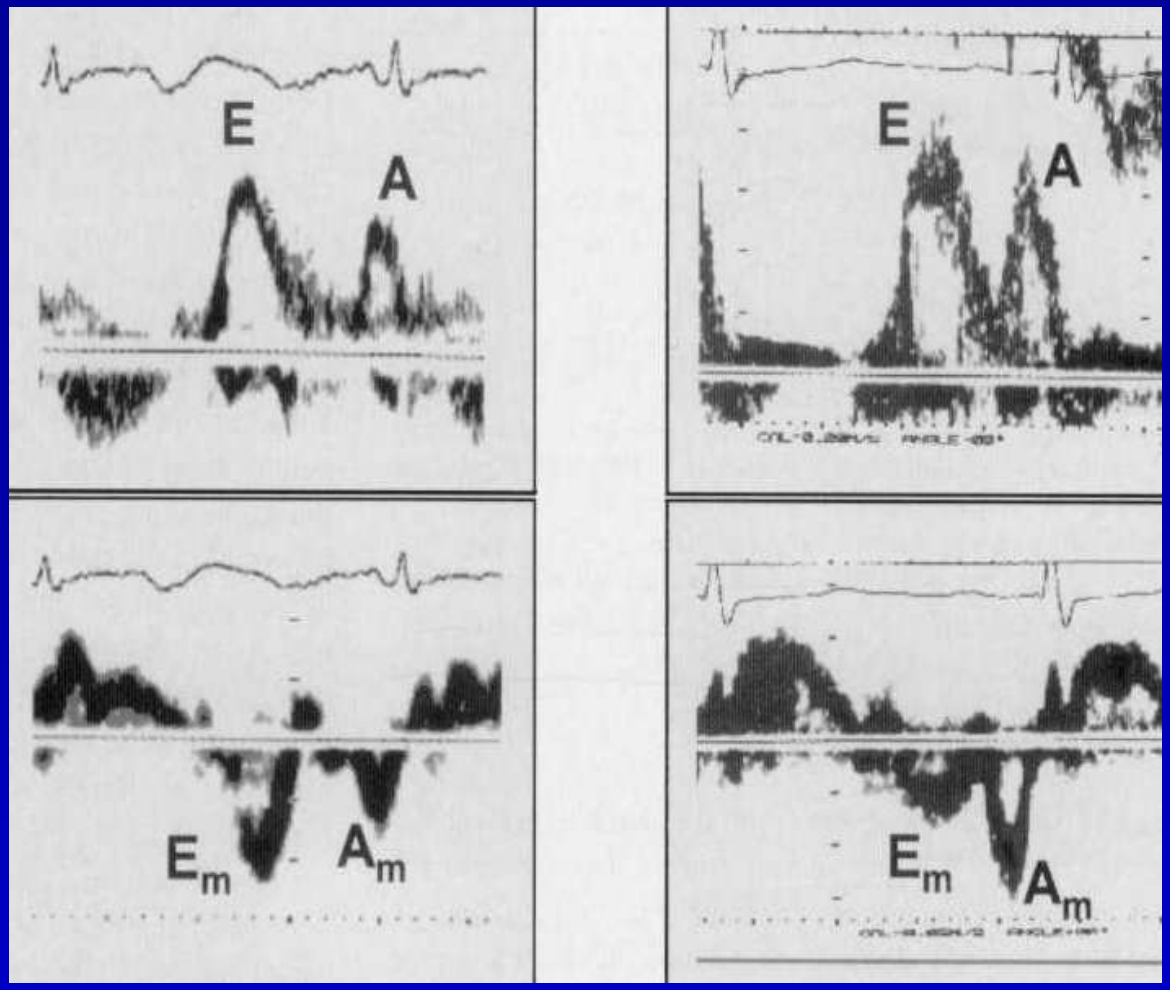
Tissue Doppler Echocardiography in Diastolic Function



Garcia, JACC 1998; 32:865

Pulsed
Doppler
A-4C
LVIT

Tissue
Doppler
Echocardiography
A-4C
MV annulus



Normal
Healthy
Volunteer

Pseudonormalization
Severe Aortic Stenosis

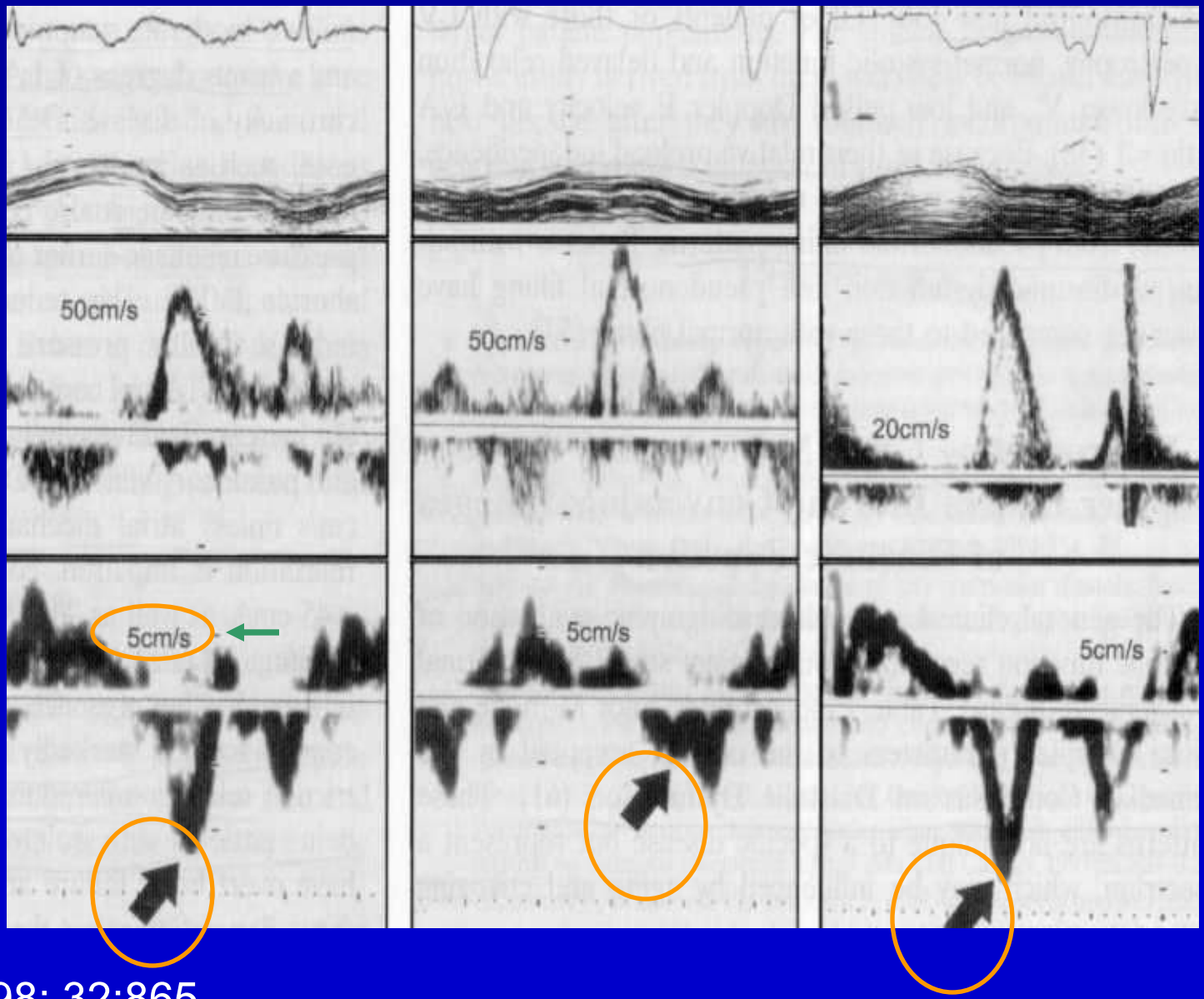
Garcia, JACC 1998; 32:865

Normal Restriction Constriction

M-mode Mitral Annulus

PW Doppler LVIT

Tissue Doppler Axial Velocity



Garcia, JACC 1998; 32:865

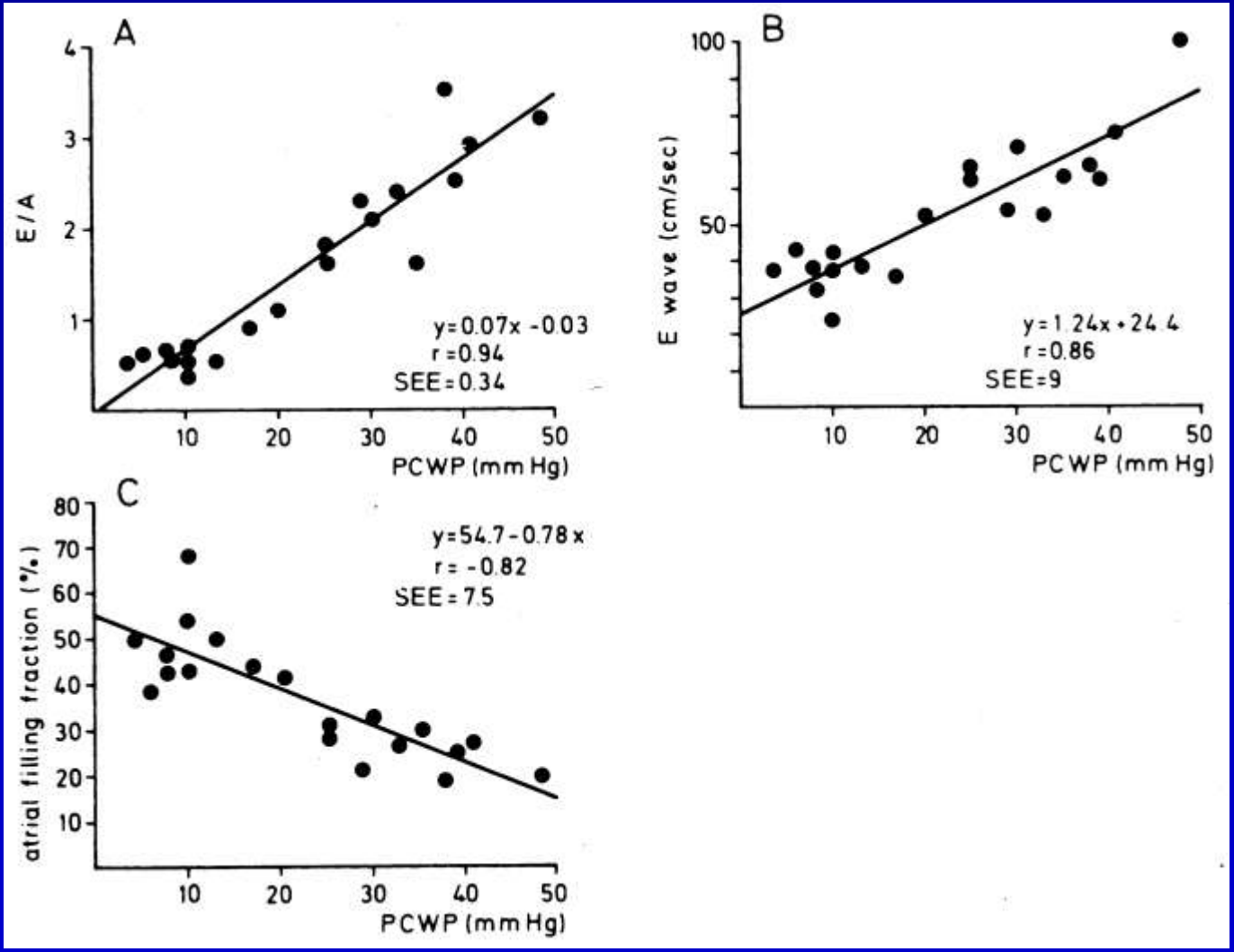
Measures of Elevated LV Filling Pressure

- LVIT E/A >2
- LVIT Edeceltime<150ms
- Short IVRT
- PV S/D <<1
- PVAr>MVAdur
- LAE, low LA EF, atrial septum bulge to right in systole
- LVE

- Caveats: Better if LV EF is low; none is truly reliable; correlation with which measure – LVEDP-Z, PCWP, LV preA, mean LA

Estimating LV Filling Pressure

34 patients with DCM



From Vanoverschelde JJ et al. J Am Coll Cardiol 1990;15:1288.

Tissue Doppler Imaging (Doppler myocardial imaging, DMI) of AV Ring

- Differentiating constriction from restriction
  - 2D echo informs on ventricular function and pericardial calcification
  - PW Doppler of ventricular filling usually differentiates
  - TDI is reported to differentiate, but exceptions are reported now (2 patients with constriction and low early TDI movement and hyperdynamic movement of the apex, a structure that usually is stationary)

Arnold MF et al. J Am Soc Echocardiogr 2001;14:391

Stages of Diastolic Dysfunction

	Normal (young)	Normal (adult)	Delayed Relaxation	Pseudonormal Filling	Restrictive Filling
E/A (cm/s)	>1	>1	<1	1-2	>2
DT (ms)	<220	<220	>220	150-200	<150
IVRT (ms)	<100	<100	>100	60-100	<60
S/D	<1	≥1	≥1	<1	<1
AR (cm/s)	<35	<35	<35	≥35	≥25
Vp (cm/s)	>55	>45	<45	<45	<45
Em (cm/s)	>10	>8	<8	<8	<8

Garcia, JACC 1998; 32:865

Stages of Diastolic Dysfunction

	Normal (young)	Normal (adult)	Delayed Relaxation	Pseudonormal Filling	Restrictive Filling
E/A (cm/s)	>1	>1	<1	1-2	>2
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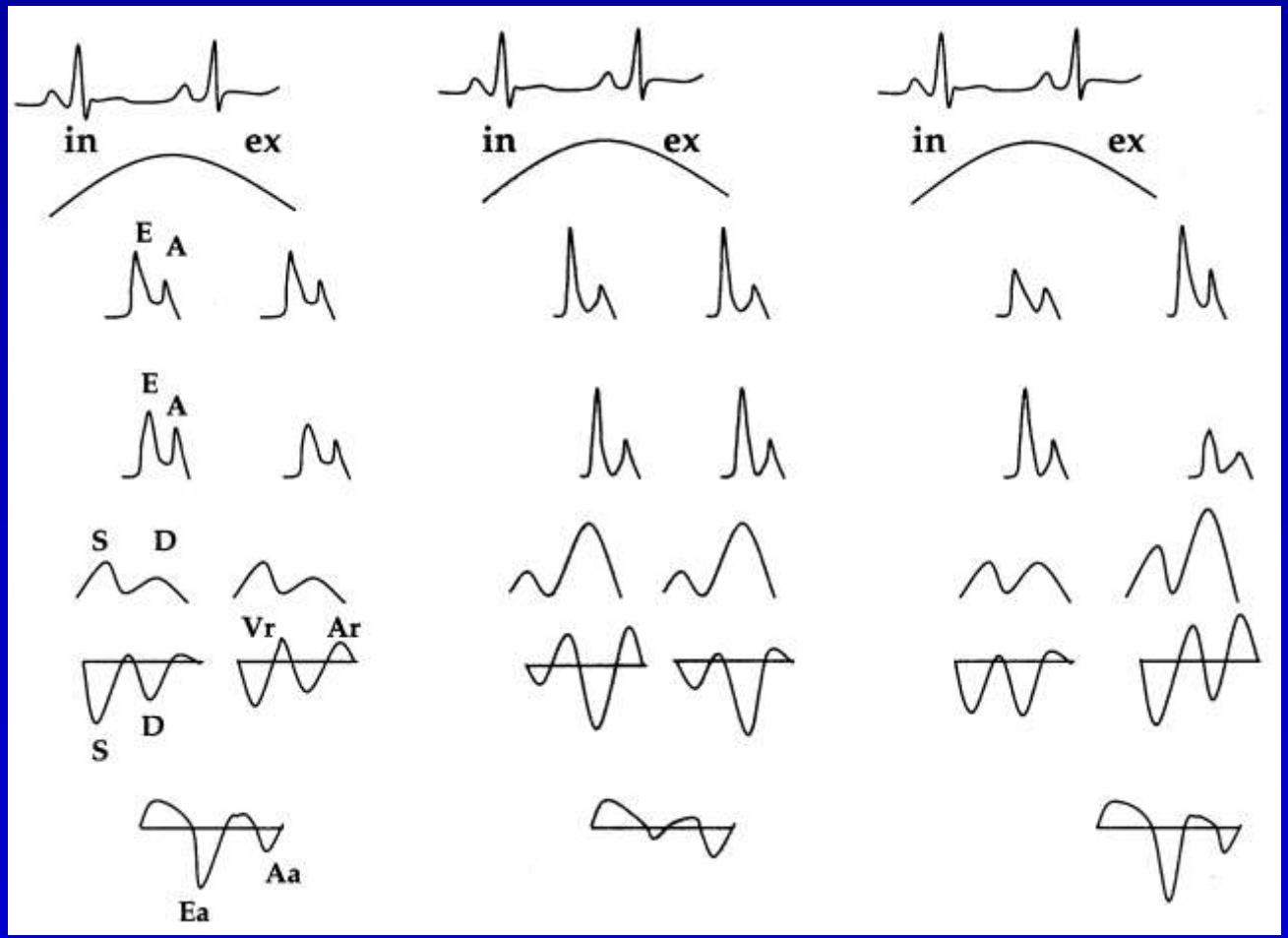
S/D	<1	≥1	≥1	<1	<1
AR (cm/s)	<35	<35	<35	≥35	≥25
Vp (cm/s)	>55	>45	<45	<45	<45
Em (cm/s)	>10	>8	<8	<8	<8

Garcia, JACC 1998; 32:865

Differentiation of Diastolic Problems

	Normal	Restrictive Cardiomyopathy	Constrictive Pericarditis
ECG			
Resp			
MV flow			
TV flow			
PV flow			
HV flow			
DT image			

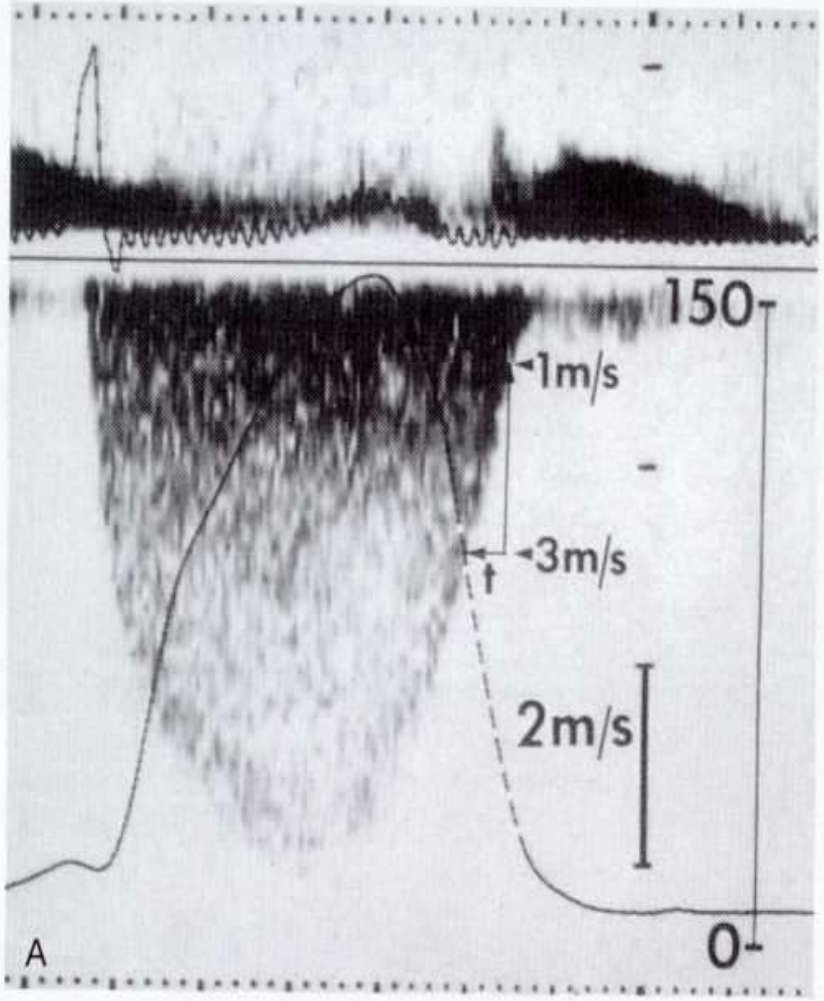
Hoit, Fig 68-2, From Hurst, 2001

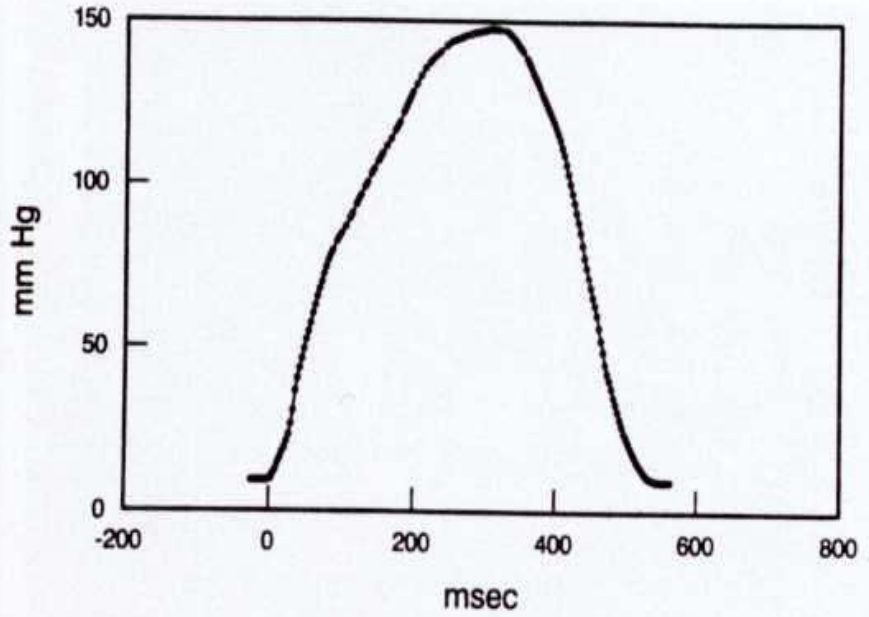
COPD and Diastole: RV and LV

- 48 patients with severe COPD
  - Group 1: 25 pulmonary hypertension
  - Group 2: 23 normal PA pressure
  - Group 3: 59 normal controls
- Pulmonary hypertension:
  - Lower TV and MV E, Higher TV and MV A, longer IVRT and slower propagation velocity than Groups 2 or 3, and no difference between group 2 and 3.

Ozer N, et al. J Am Soc Echocardiogr 2001;14:557-61

Mitral Regurgitation to estimate tau (relaxation constant)





Digitized LV pressure estimate from MR Doppler

Smith, Mikel, in Otto, 1997, from Nishimura RA et al. Circulation 1993;88:146.

Review References

- Oh JK et al. The noninvasive assessment of left ventricular diastolic function with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 1997;10:246-70
- Appleton CP et al. Doppler evaluation of left and right ventricular diastolic function: a technical guide for obtaining optimal flow velocity recordings. J Am Soc Echocardiogr 1997;10:271-91
- Nishimura RA et al. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta stone. J Am Coll Cardiol 1997;30:8-18
- Garcia MJ et al. New Doppler echocardiographic applications for the study of diastolic function. J Am Coll Cardiol 1998;32:865-75
- Smith MD. Left ventricular diastolic function: clinical utility of Doppler echocardiography. Ch. 3 in Otto CM. The Practice of Clinical Echocardiography WB Saunders, 1997
- Pai RG. Newer Doppler measures of left ventricular diastolic function. Clin Cardiol 1996;19:277
- Rakowski H et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography. J Am Soc Echocardiogr 1996;9:736

Pulmonary Venous Flow Pattern

- LV preload and systolic and diastolic function
  - Increased LA pressure - more S dominance if LV systolic function is preserved, lower S if LV systolic dysfunction
  - Impaired relaxation - lower D wave and more S, corresponding to lower MV E
  - Pseudonormal - dominant D wave and larger Ar wave (lower LV compliance)
  - Restrictive has large D and rapid D deceleration, Ar is variable
- RV systolic function
- SBP and peripheral vascular resistance
- Age increases systolic dominance and maybe Ar
- Mitral regurgitation* reduces S wave, reverses if severe MR
- Large ASD causes single continuous antegrade wave and diminished AR wave**

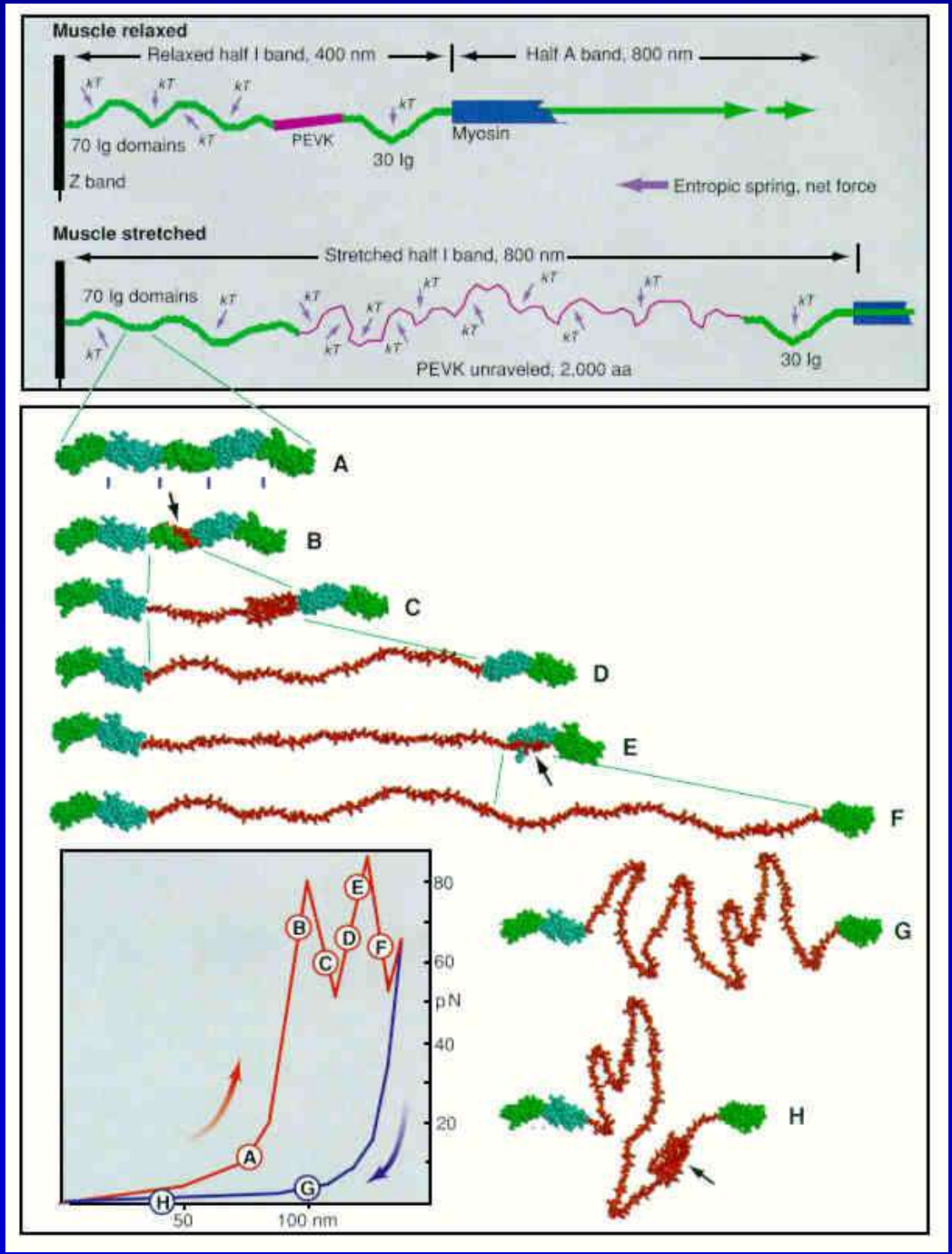
*Rossi A, et al. J Am Soc Echocardiogr 2001;14:562
**Saric M, et al. J Am Soc Echocardiogr 2001;14:386

Titin in Diastolic Function

- Also called connectin, after actin and myosin the third most abundant muscle protein, about 10% of muscle protein
- Molecular scaffolding for thick filament formation (highly ordered and tightly attached to thick filament in the A band)
- Giant protein (3,000 kD) providing most of the elasticity of resting striated muscle, especially the I-band region (with thin filament)
- Resting length 1 micrometer spanning from Z to M lines
- Structure: 300 Ig and related FNIII repeats (account for almost 90% of its mass), and PEVK domain (Pro-Glu-Val-Lys) that makes a polyproline helix (PPII)
- Abnormality in titin gene has been implicated in familial hypertrophic cardiomyopathy*

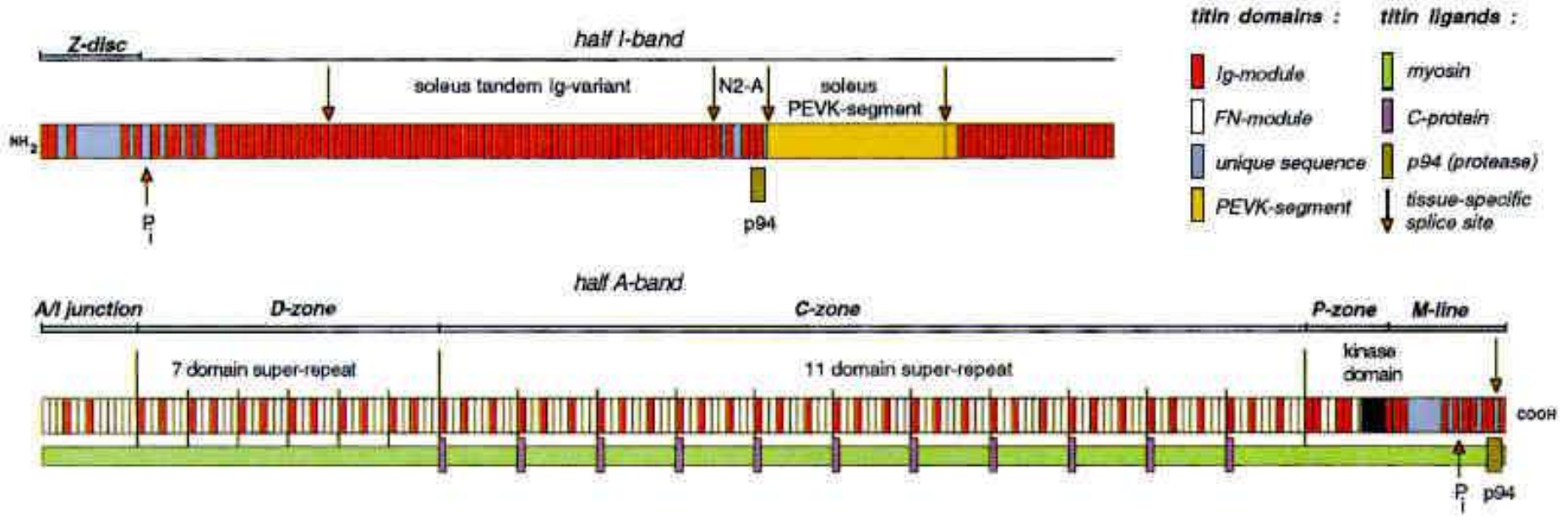
Labeit S et al. Circulation Research 1997;80:290
*Kimura A et al. Journal of Cardiology 2001;37Suppl 1:139

Titin in Diastolic Function



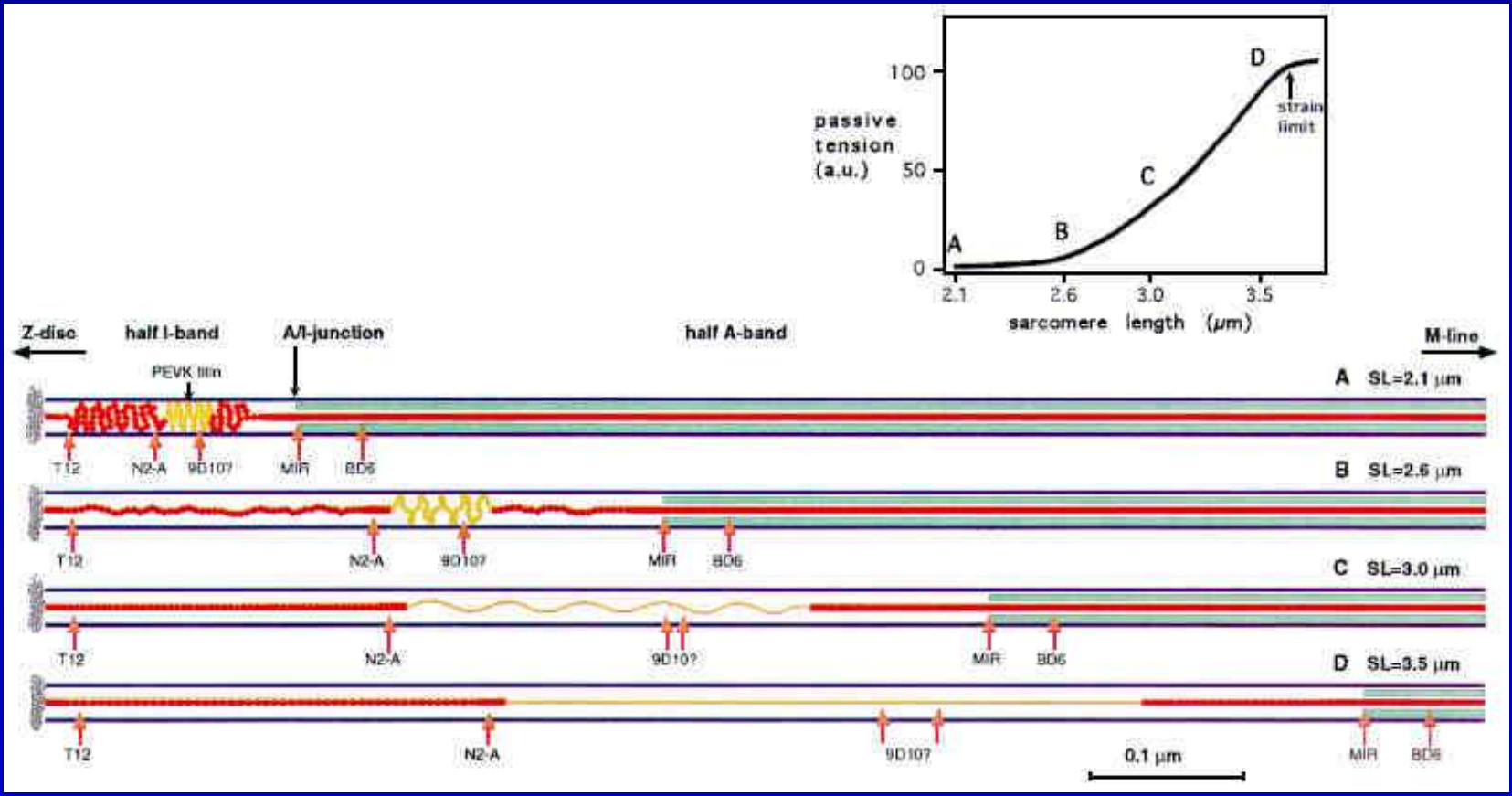
Erickson HP.
Science 1997;276:1090

Titin Structure



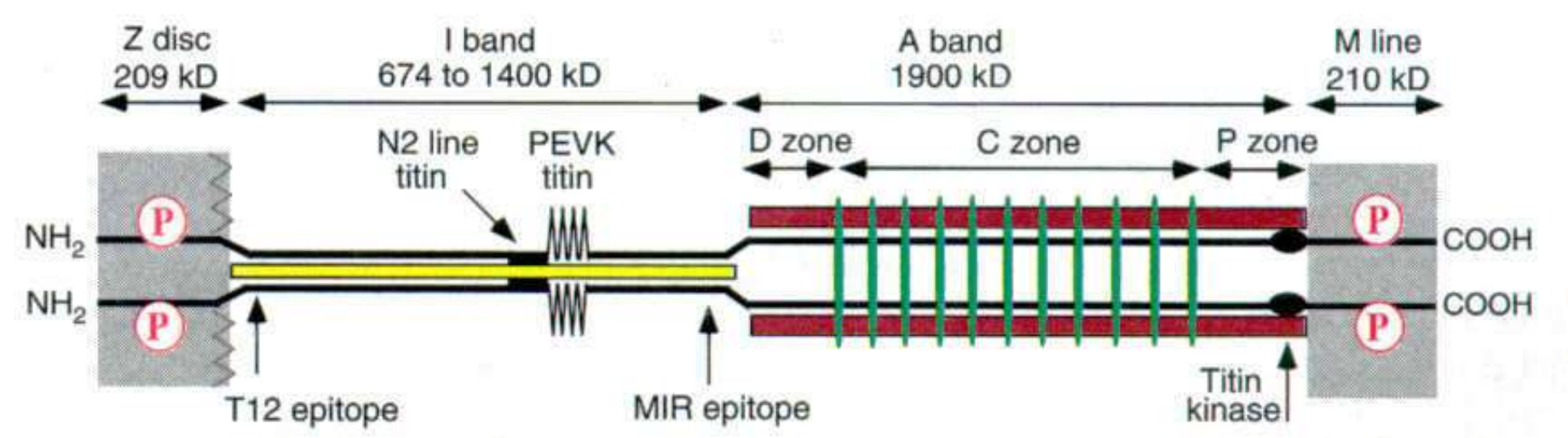
Domain architecture and sarcomeric layout of the titin filament. The domain structure of the human soleus titin, as predicted by its 100-kb mRNA, is shown. The 3.7-MD soleus titin peptide contains 297 copies of 100-residue repeats, which are members of the Ig and FN3 superfamilies. Each of these domains folds into a 10- to 12-kD small globular subunit, as shown by structural studies. Specific for the I-band segment of titin are strings of tandemly repeated Ig domains (tandem-Ig titin) and the "PEVK domain," rich in proline, glutamate, valine, and lysine residues. The tandem-Ig and the PEVK region of titin represent those parts of the titin filament that extend during physiological amounts of stretch. Specific for the A-band titin are regular patterns of Ig and FN3 domains, referred to as "super repeats." These super repeats provide multiple and structurally ordered binding sites for myosin and C protein. In addition to the Ig/FN3 repeats and the PEVK region of titin, 8% to 10% of titin's mass is formed by unique sequence insertions. Among the encoded peptides are phosphorylation motifs (P_i) and a serine/threonine kinase. The mapped calpain p94-binding sites are shown. Arrows above the domain pattern indicate the sites

Titin Structure



Current model of titin extension with sarcomere stretch in psoas muscle. The inset shows a typical passive length-tension curve of single psoas myofibrils, with the letters A through D referring to the sarcomere lengths depicted in the main figure. It should be pointed out that this model proposed for psoas titin extension may not adequately address the situation in cardiac muscle, where the contribution of the short PEVK segment to I-band titin extensibility is very small. In cardiac sarcomeres, a significant passive tension increase appears shortly above slack length and seems to be correlated with extension of the tandem-Ig region. The precise mechanism of titin elasticity remains to be elucidated. Color codes are as follows: blue, actin; green, myosin; yellow, PEVK region of titin; and red, non-PEVK domains. The filled circles represent the I-band tandem-Ig modules. T12, N2-A, MIR, and BD6 are known binding sites of titin antibodies used to measure the extension

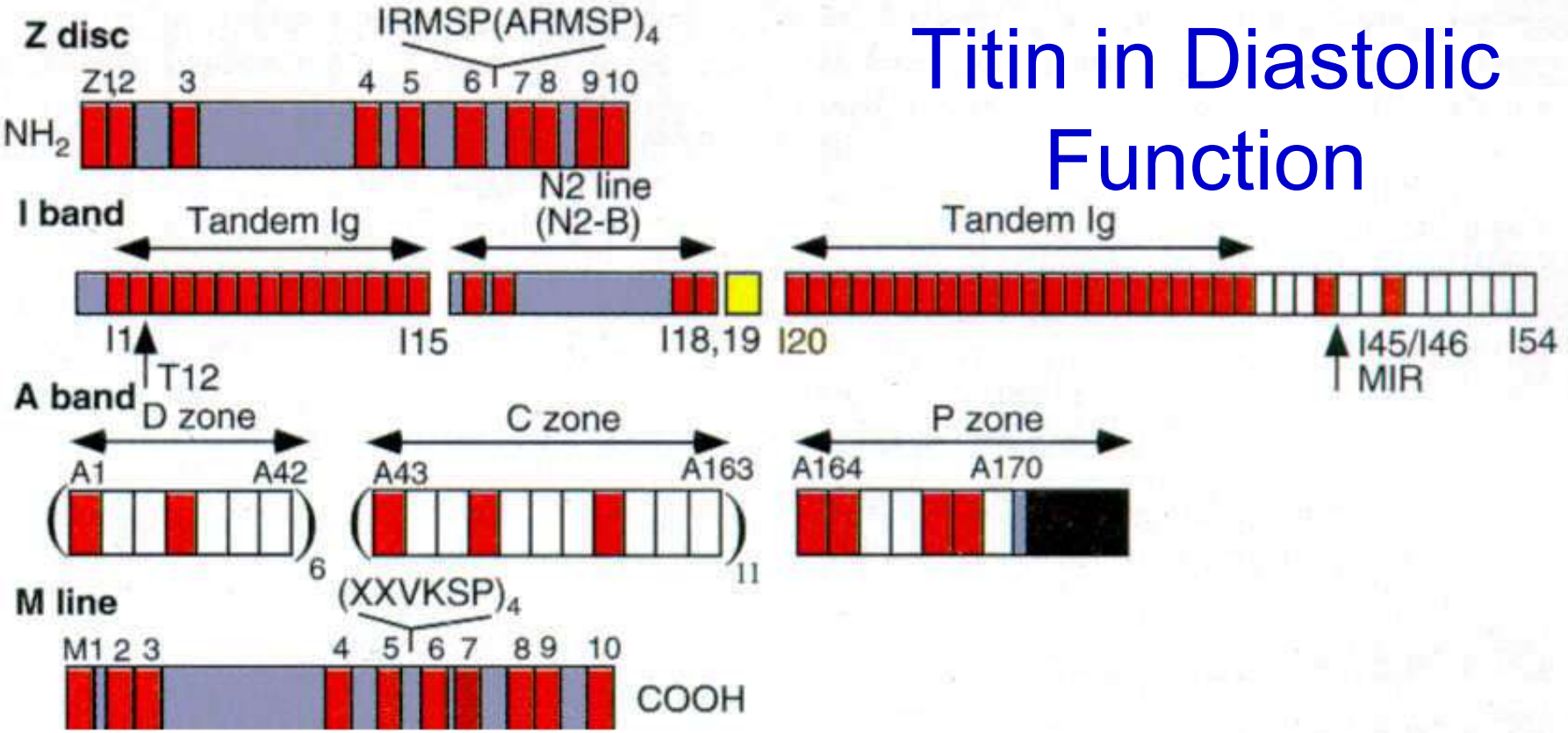
Titin in Diastolic Function



Model for titin in the sarcomere. The titin filament is shown in black, the thin filament (actin) in yellow, and the thick filament (myosin) in red. The epitopes of the titin antibodies T12 and antibodies to the MIR have been mapped in the sarcomere by immunoelectron microscopy; the positions of their epitopes in the titin sequence are known. Antibodies to the titin kinase domain react with the periphery of the M line. Therefore, it can be estimated which sections of the titin sequence are in the Z disc, I band, A band, and the M line. For the I band, the range of variation as predicted by the observed splice variants is indicated. The presumed extensible element of the I band, the PEVK element, is located between the N2 line titin and the second tandem Ig block (zig-zag pattern). Within the thick filament in the central C zone (green stripes), titin binds to both the C protein and myosin and is likely to specify the presence of 11 copies of the 430 Angstrom thick filament repeat in vertebrate striated muscles. Phosphorylation of tandemly arranged Ser-Pro repeats in the Z disc and the M line titin (red P) may control integration of the titin filament into Z discs and M lines during myogenesis

Labeit M et al. Science 1995;270:293

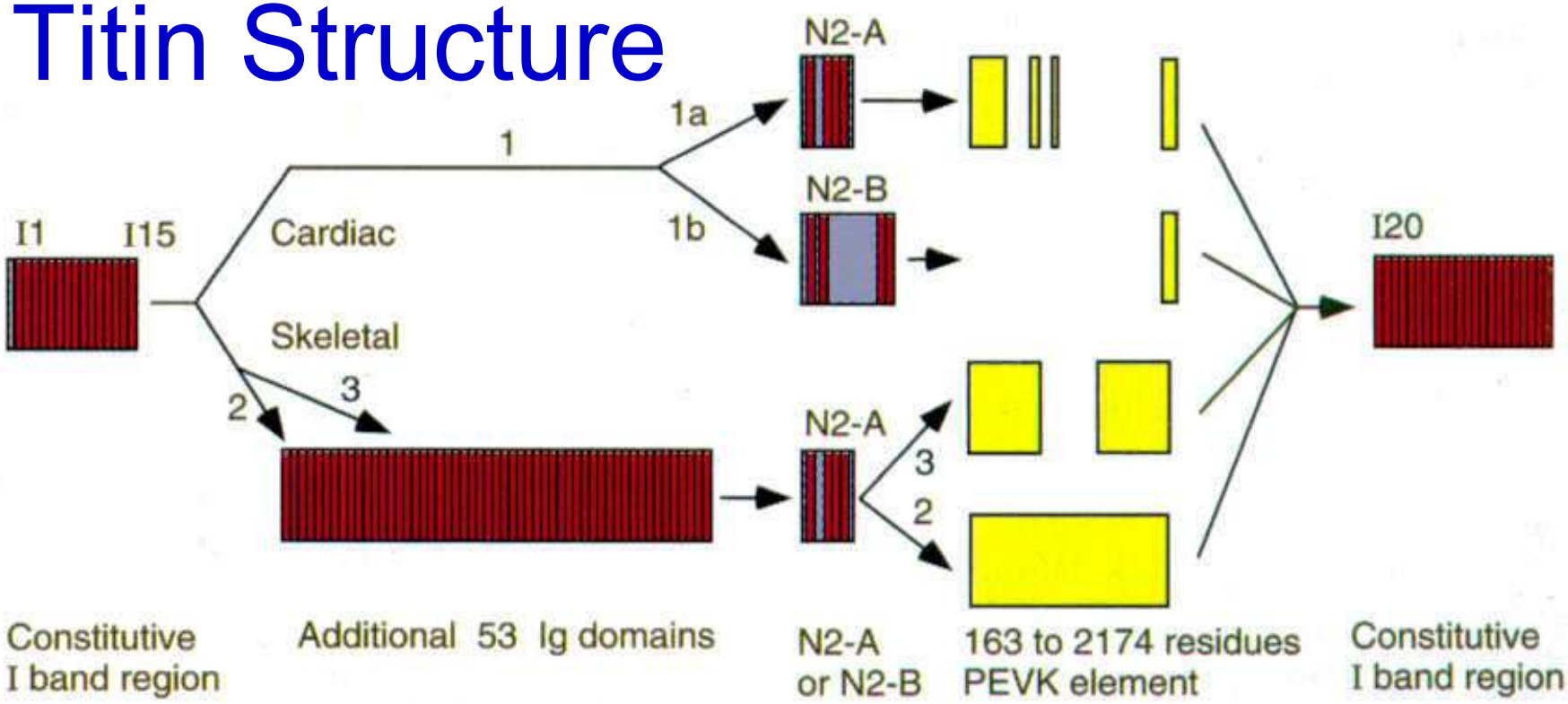
Titin in Diastolic Function



Domain structure of the cardiac titin filament. The modular architecture of cardiac titin as predicted by its full-length cDNA is shown. A total of 244 copies of 100-residue repeats (indicated by vertical rectangles) are contained, of which 112 belong to the Ig (red) domain and 132 to the FN3 (white) superfamily. The 100-residue repeats are indicated by region and position regardless of whether they are Ig or FN3 domains. The titin kinase domain is shown in black, the PEVK element (N2-B 163-residue variant; see Figure 3 in yellow. Sequences with no homology to database entries comprise 10% of the titin primary structure (blue). The epitope positions of T12 and MIR are indicated. The change in motif organization NH ($_{2\text{-terminal}}$) of T12 is proposed to be the Z disc-I band junction; the start of super-repeats COOH-terminal of MIR is proposed to be the beginning of the A band region of titin. Within the A band region, the D zone contains six copies of the seven-module super-repeat (A1 through A42); the C zone contains 11 copies of the 11-module super-repeat (A43 through A163). The positions of the tandemly repeated RMSP and VKSP motifs in the Z disc and M line region of titin are shown [29].

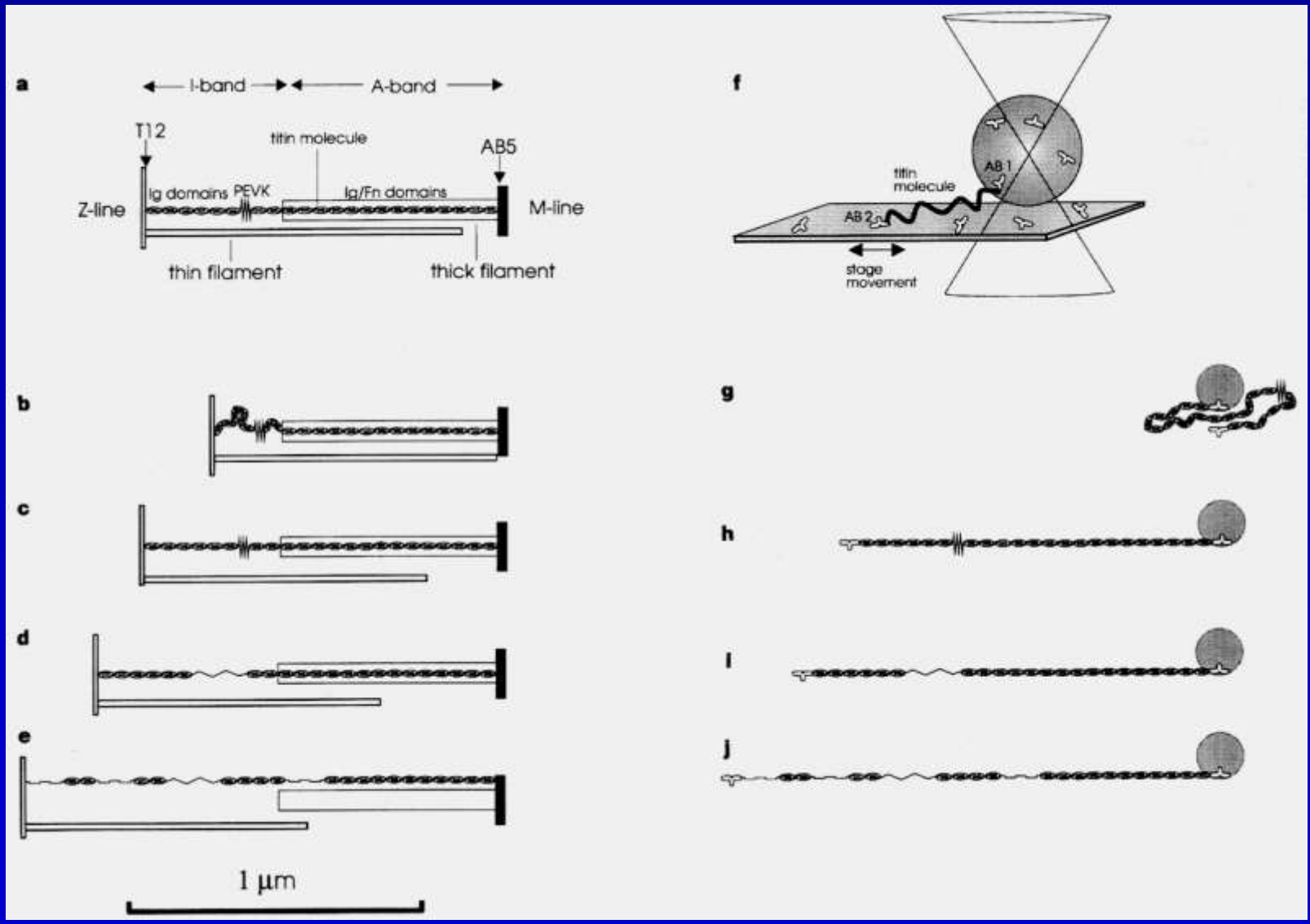
Labeit M et al. Science 1995;270:293

Titin Structure



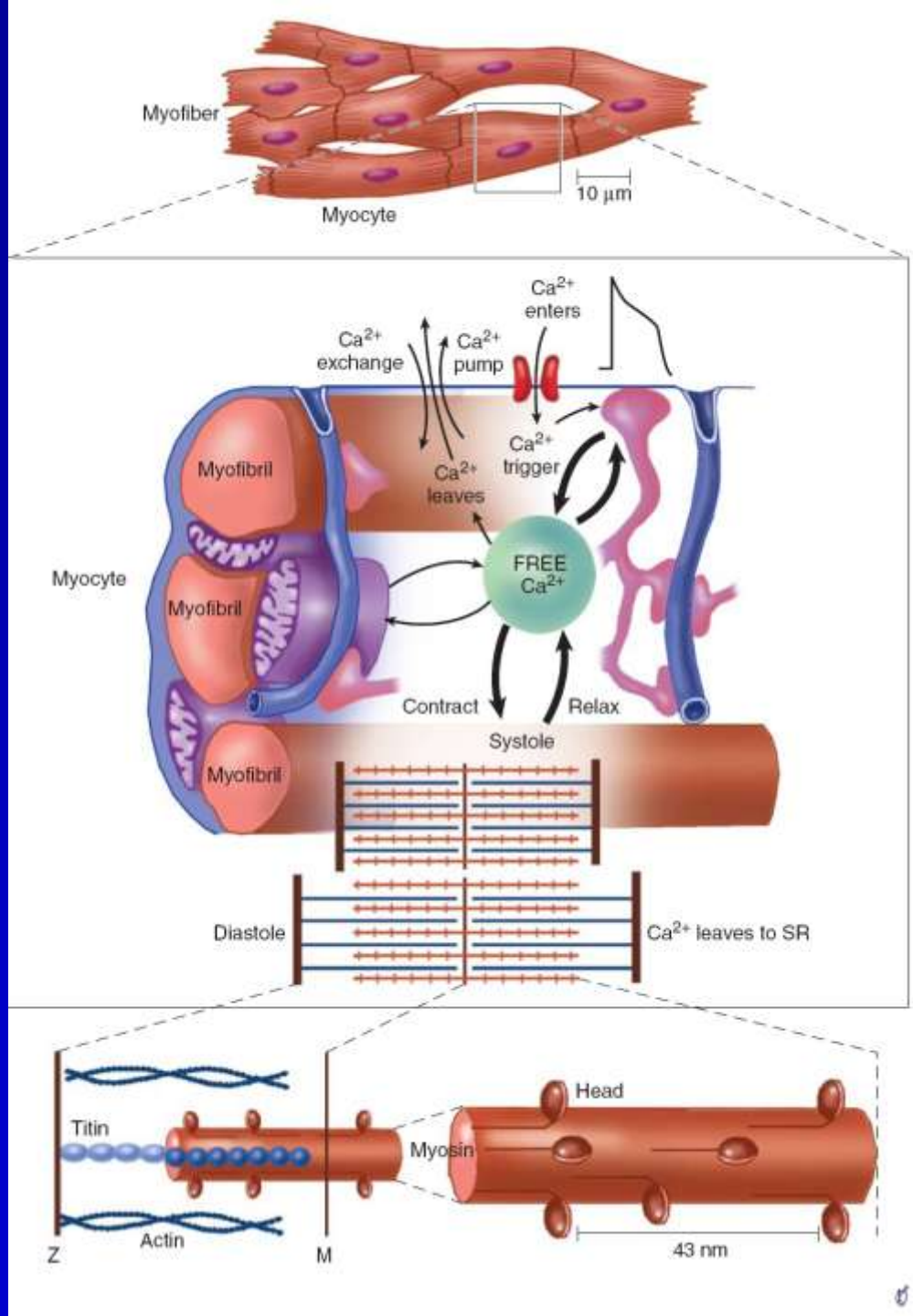
Labeit M et al. Science 1995;270:293

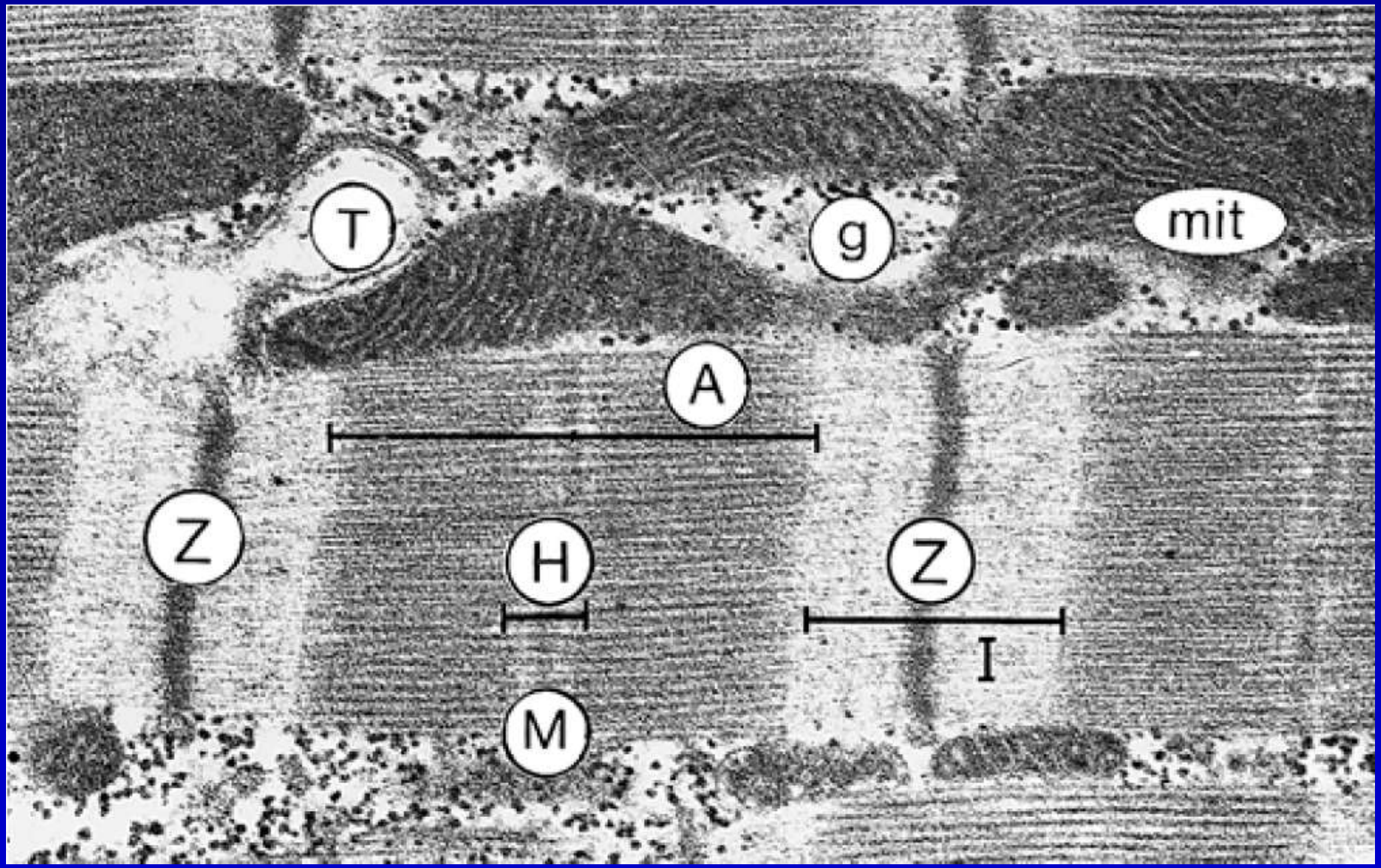
Titin in Diastolic Function



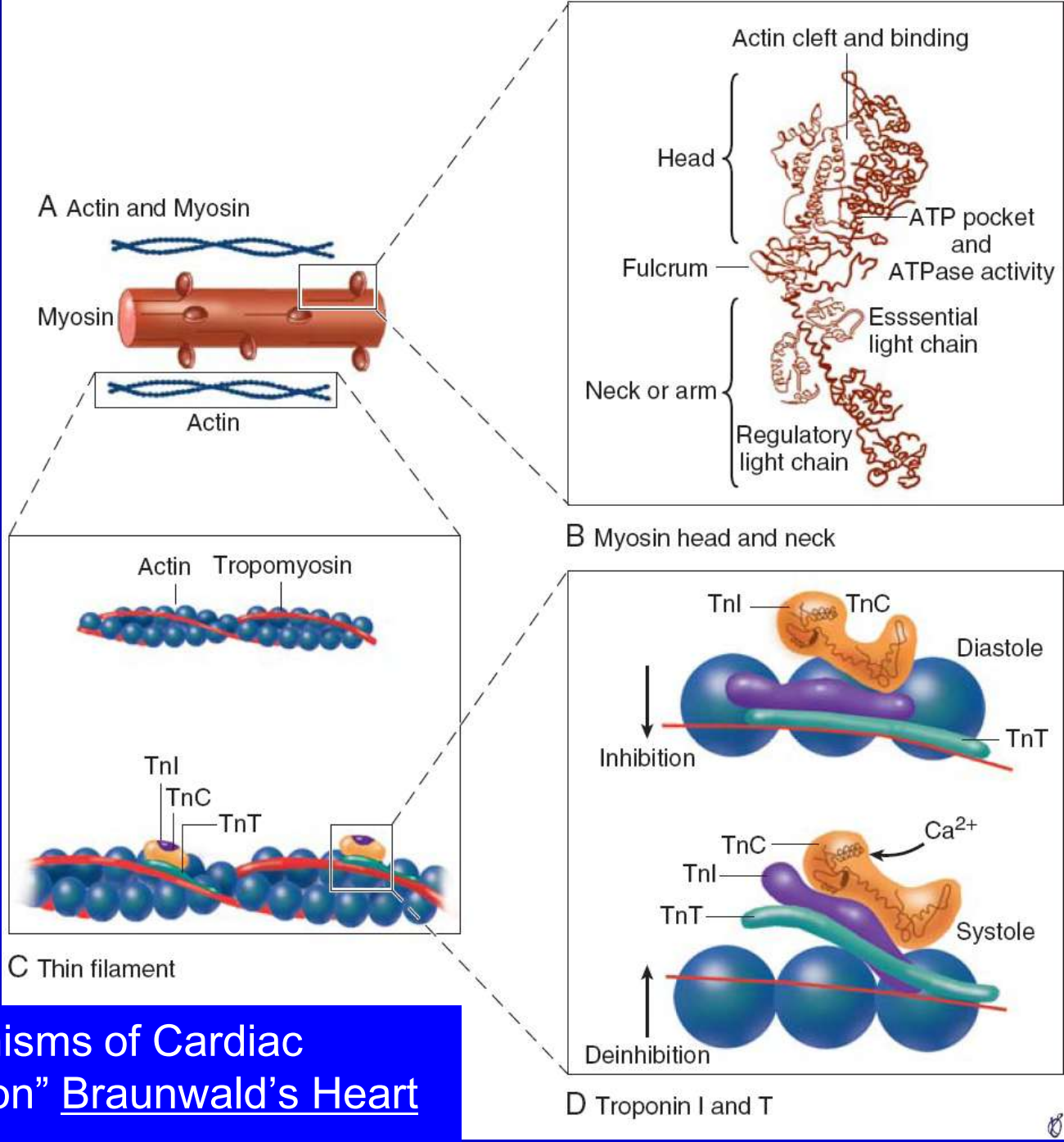
Tskhovrebova L et al. Nature, 1997;387:308.

Opie LH. Ch 19, “Mechanisms of Cardiac Contraction and Relaxation” Braunwald’s Heart Disease, 7th ed. 2004.

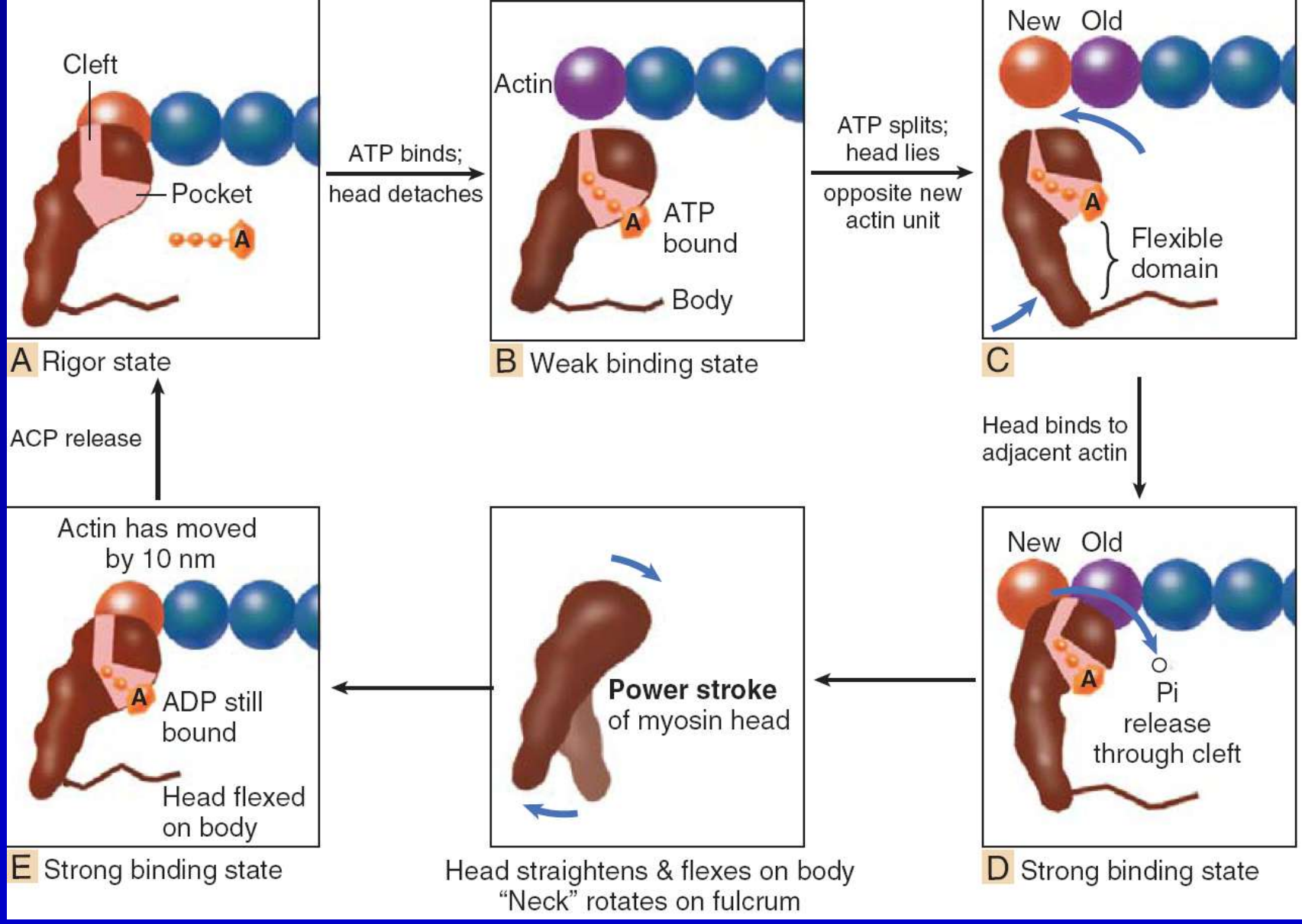




Opie LH. Ch 19, “Mechanisms of Cardiac Contraction and Relaxation” Braunwald’s Heart Disease, 7th ed. 2004.



Opie LH. Ch 19, "Mechanisms of Cardiac Contraction and Relaxation" Braunwald's Heart Disease, 7th ed. 2004.



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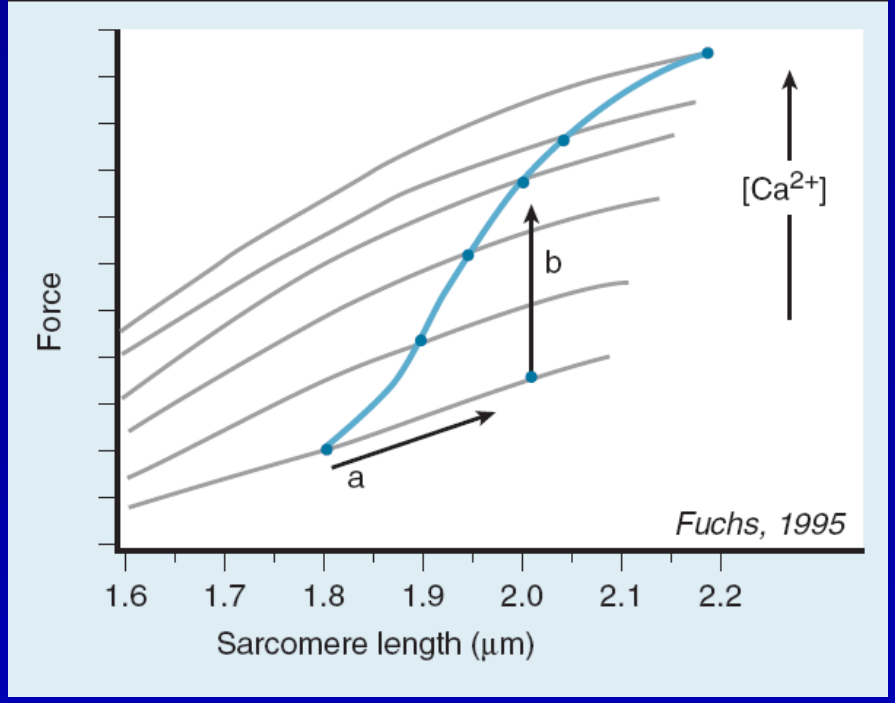

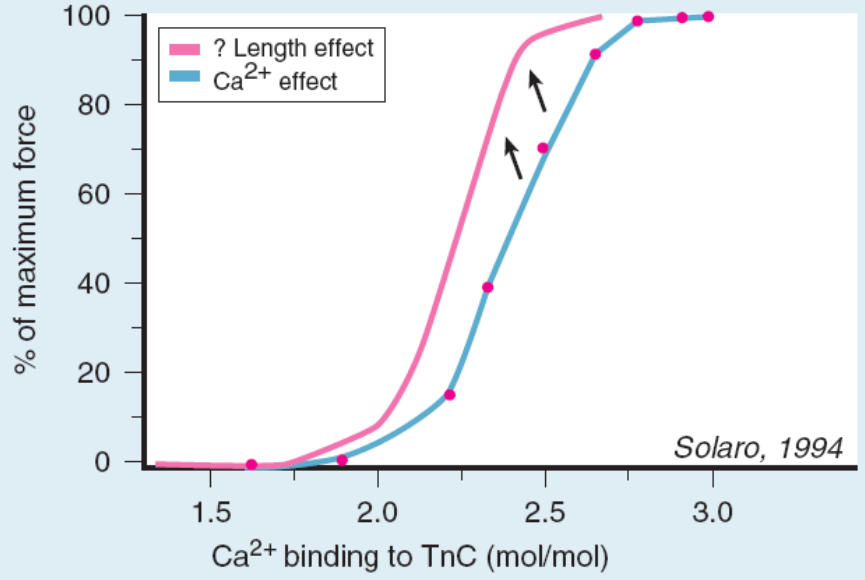

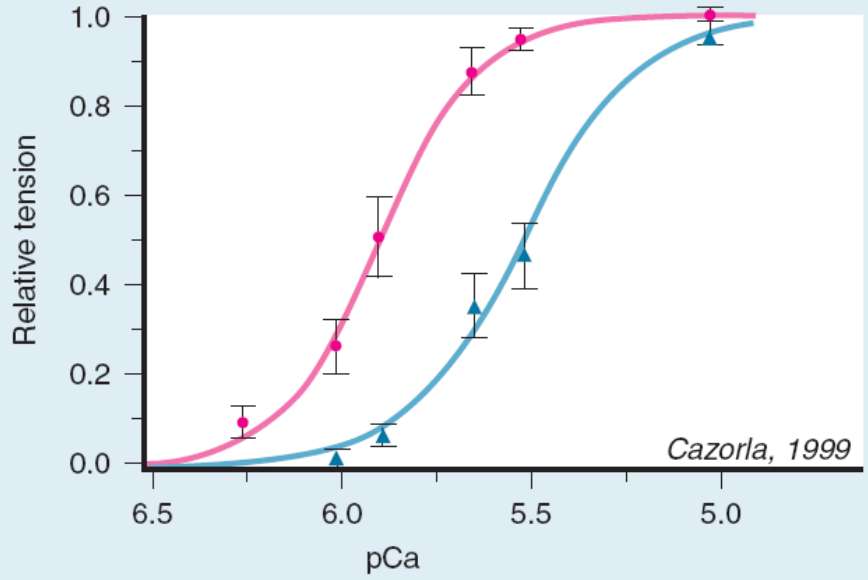

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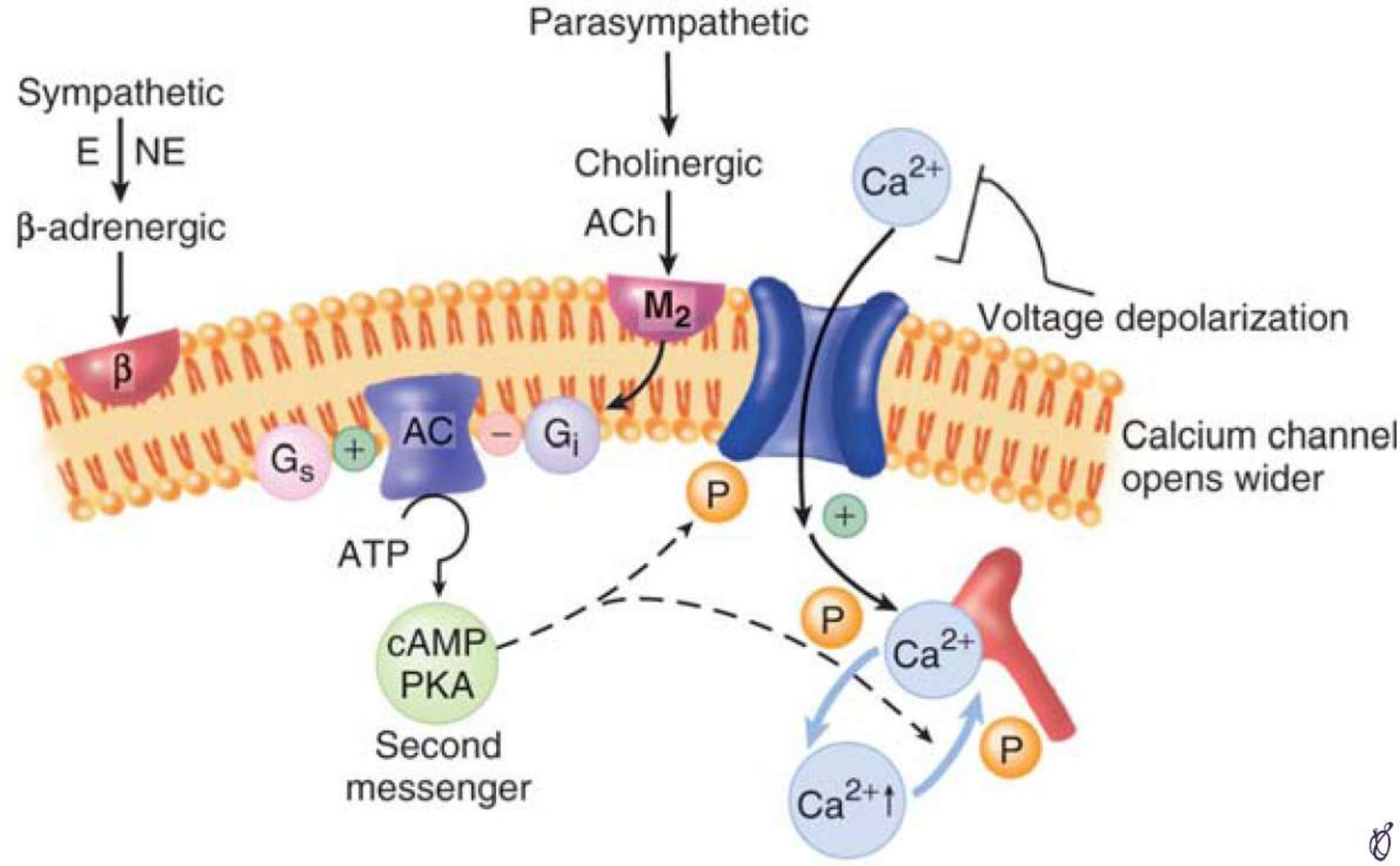

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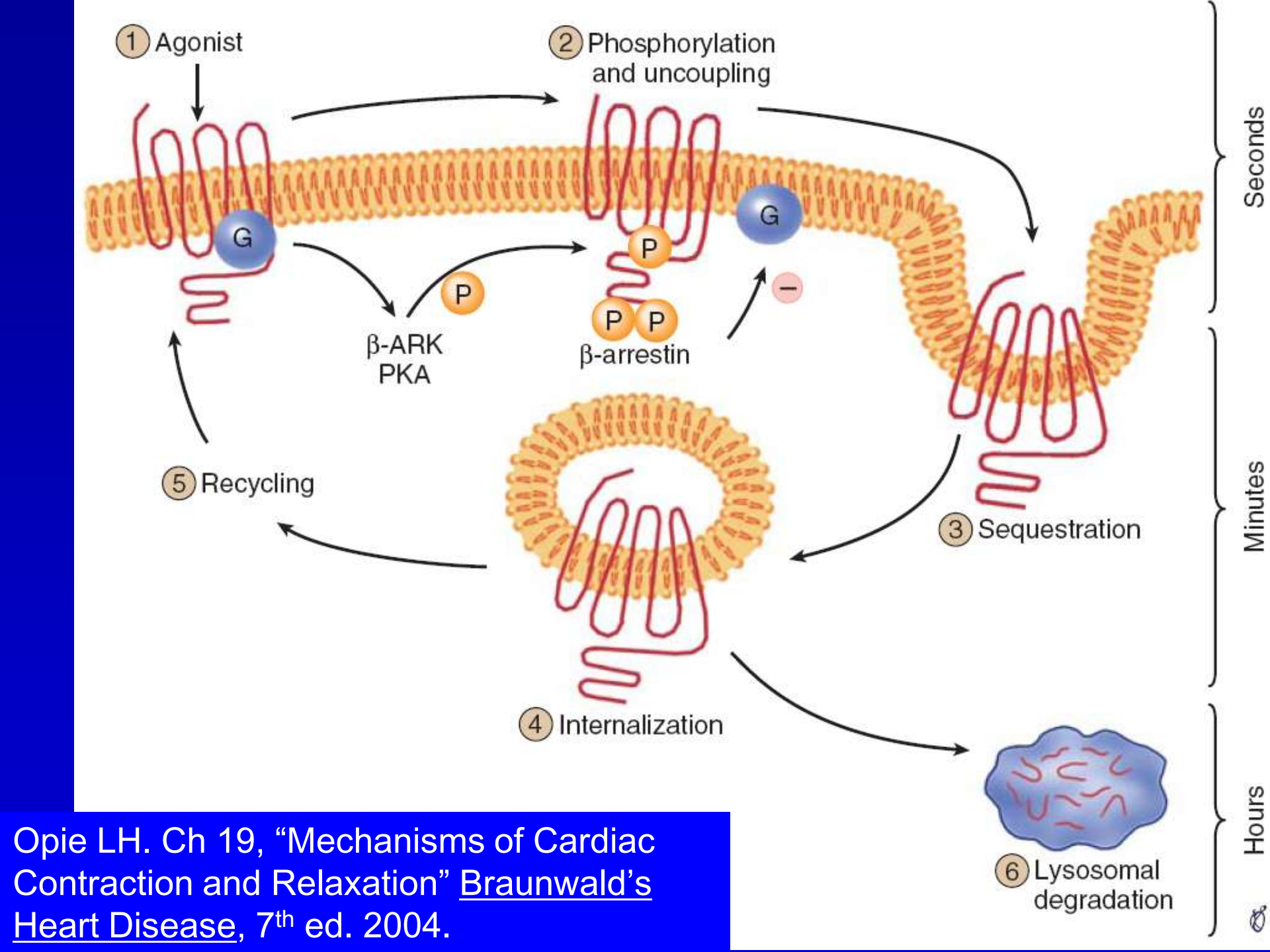

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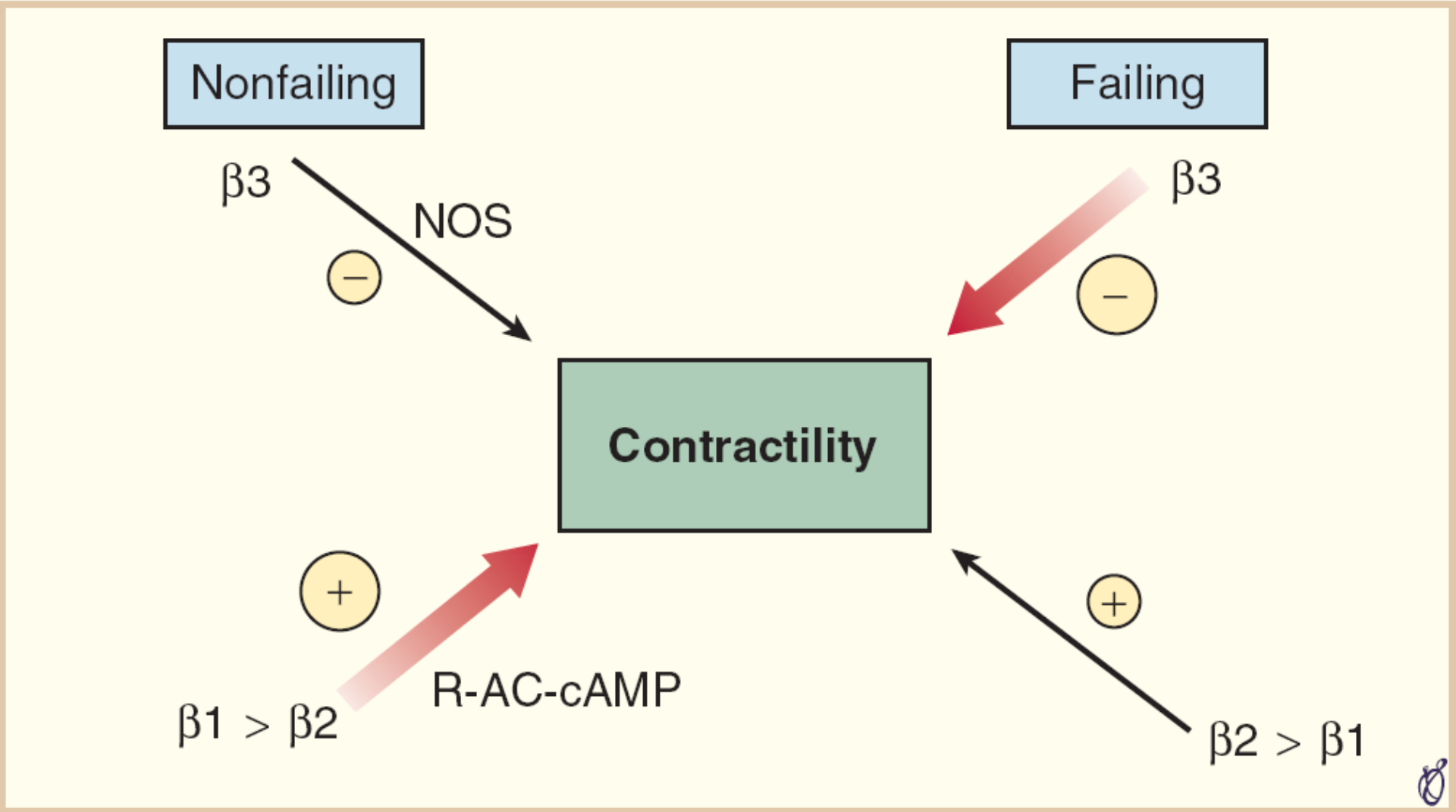

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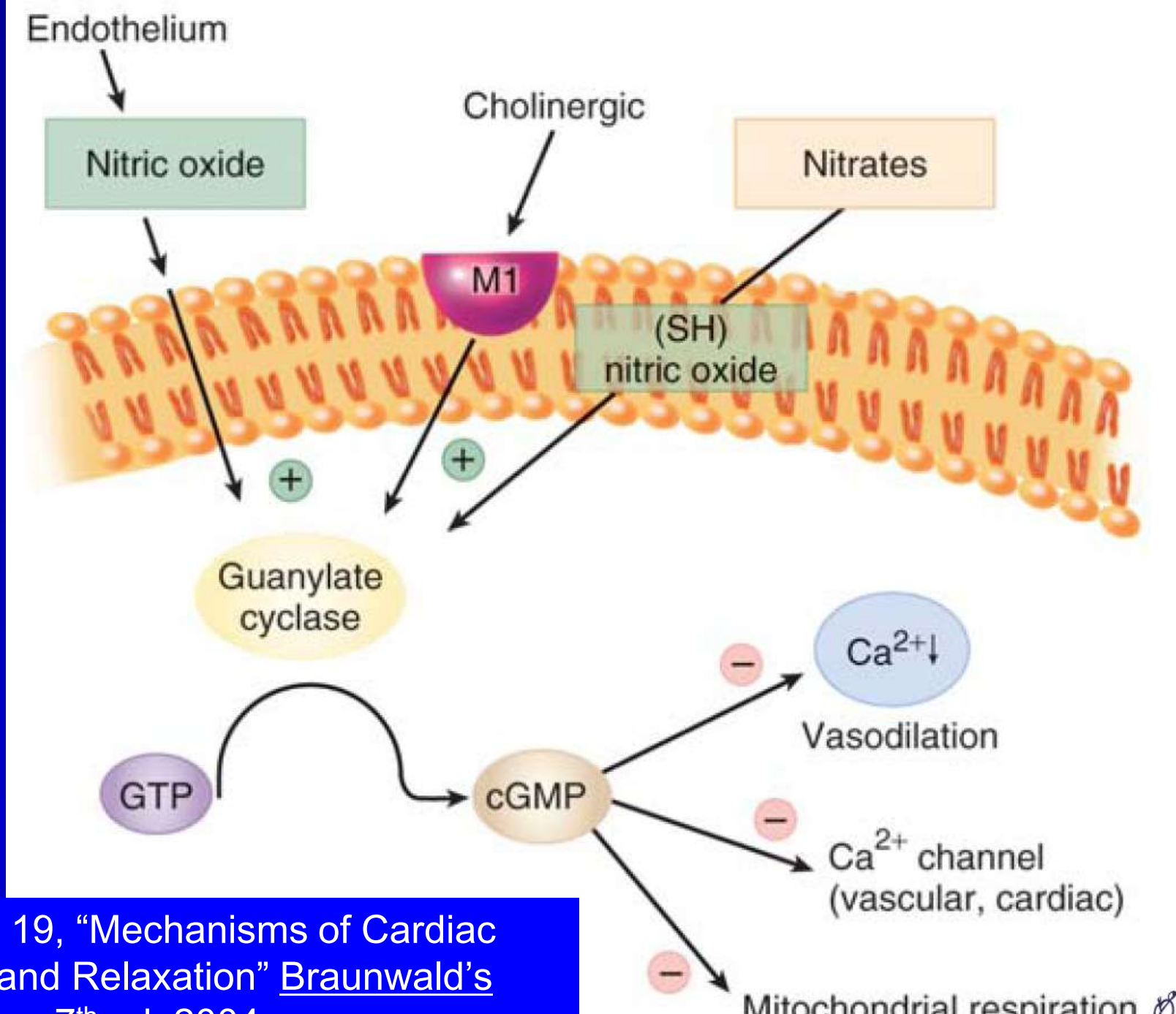

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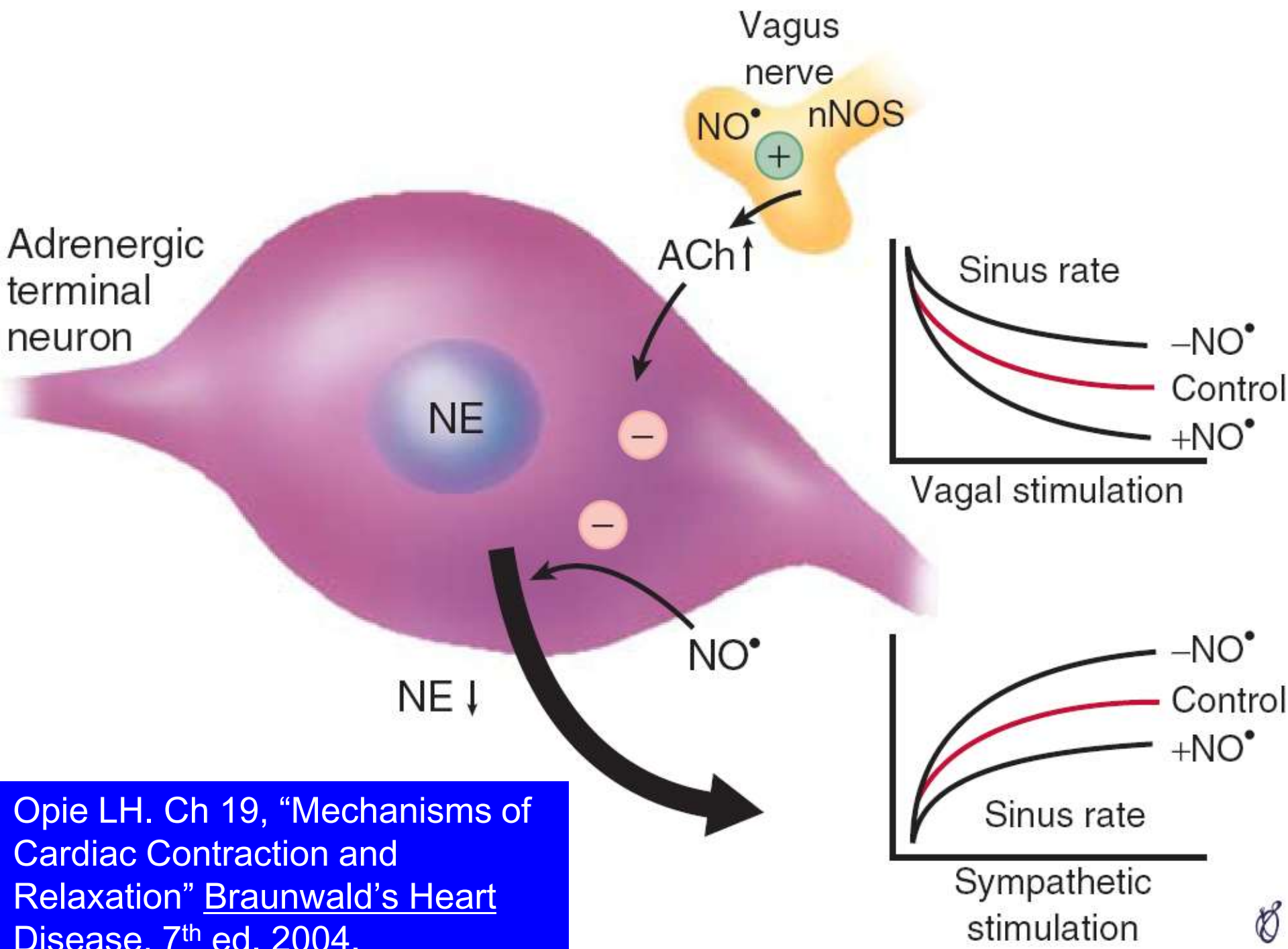

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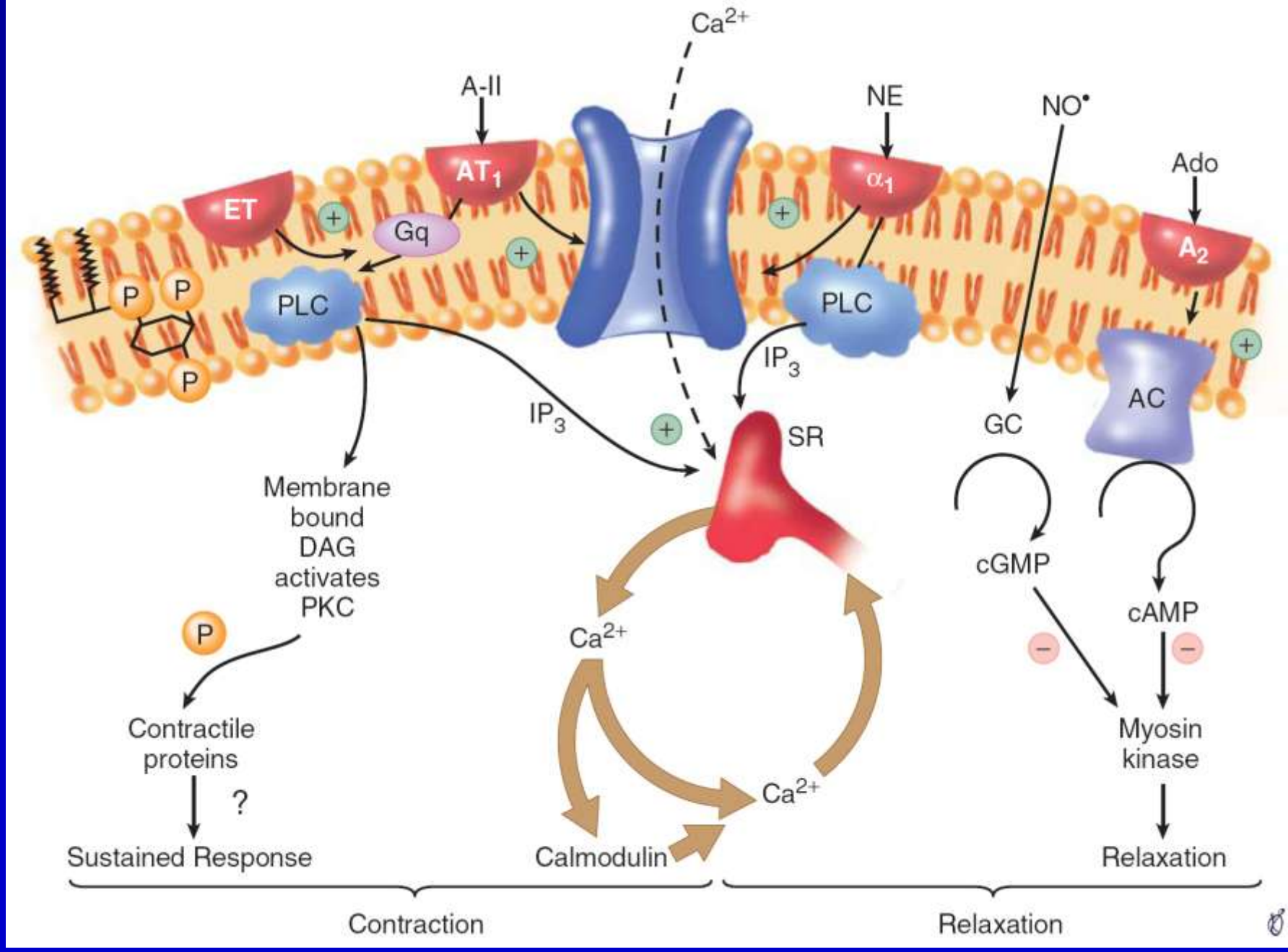

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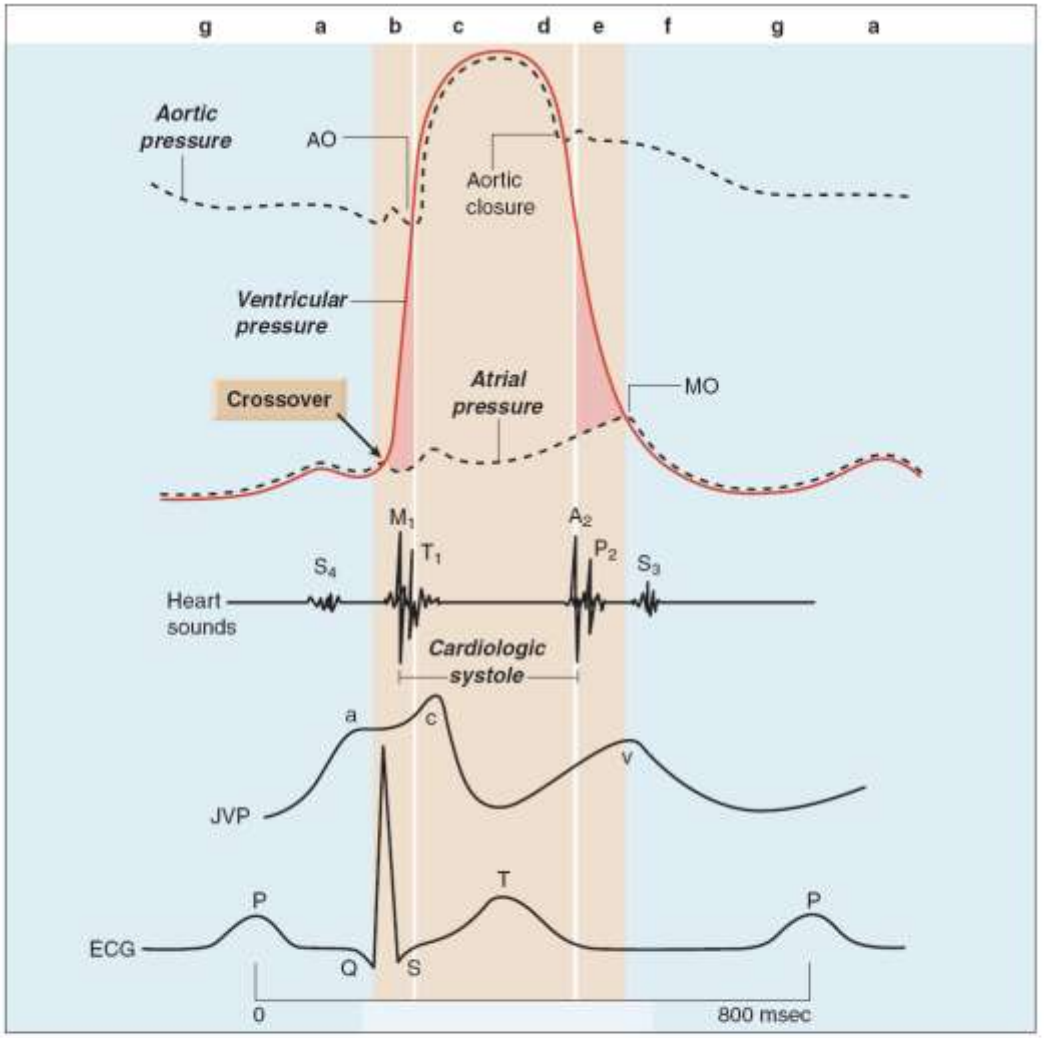

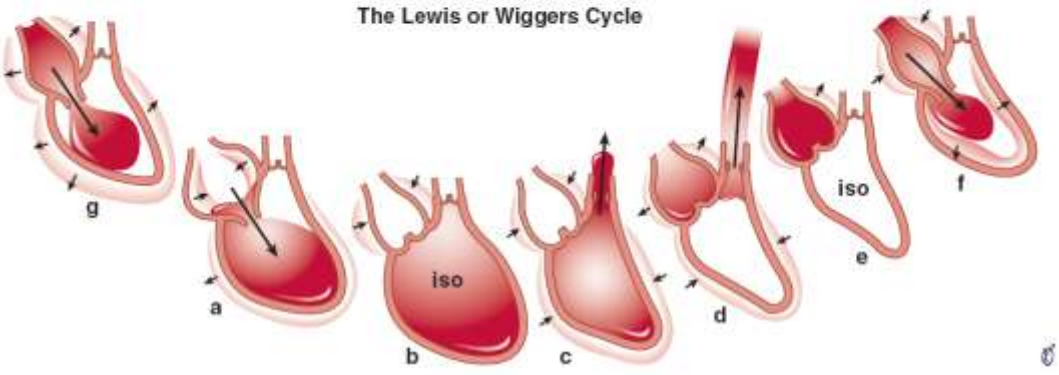

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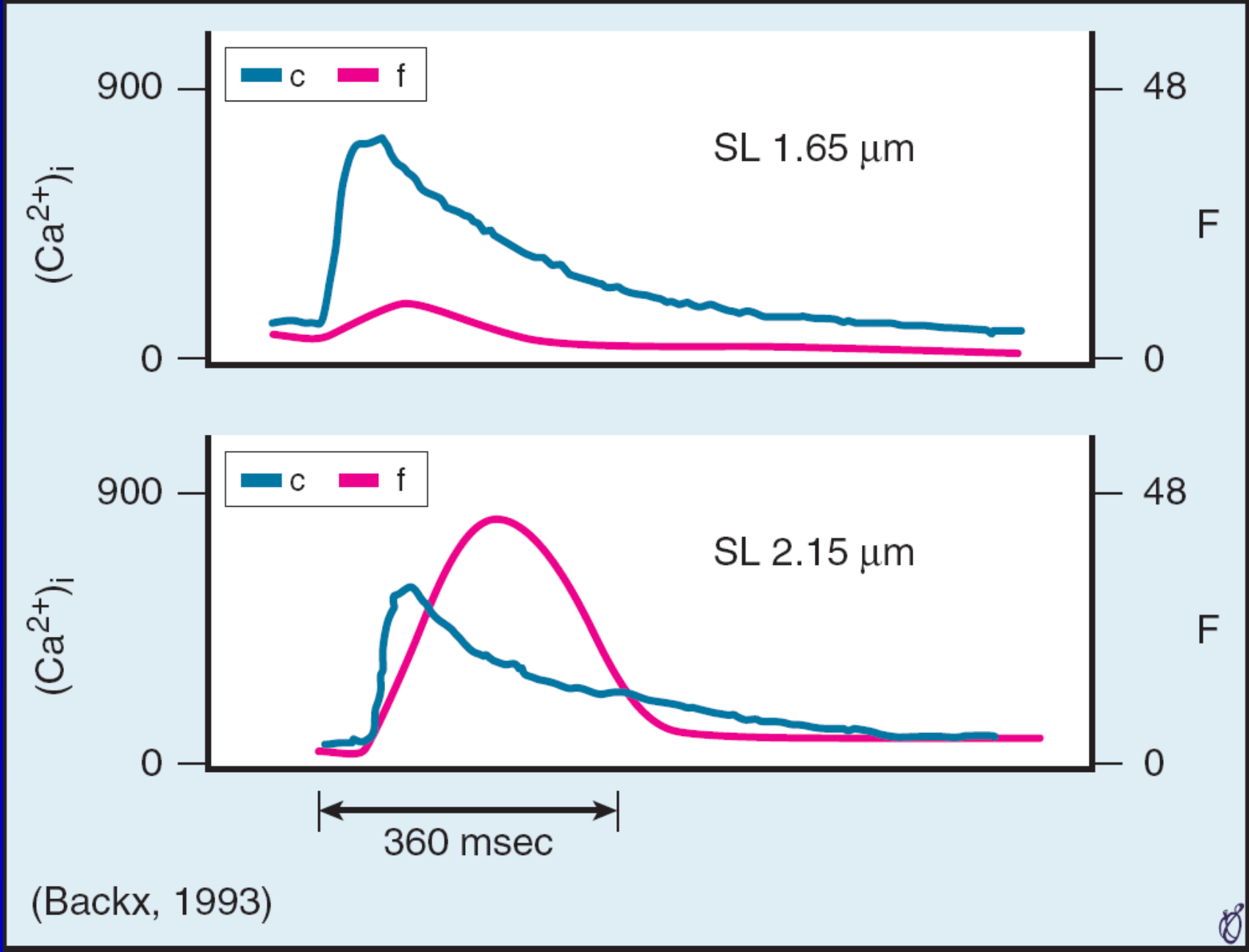

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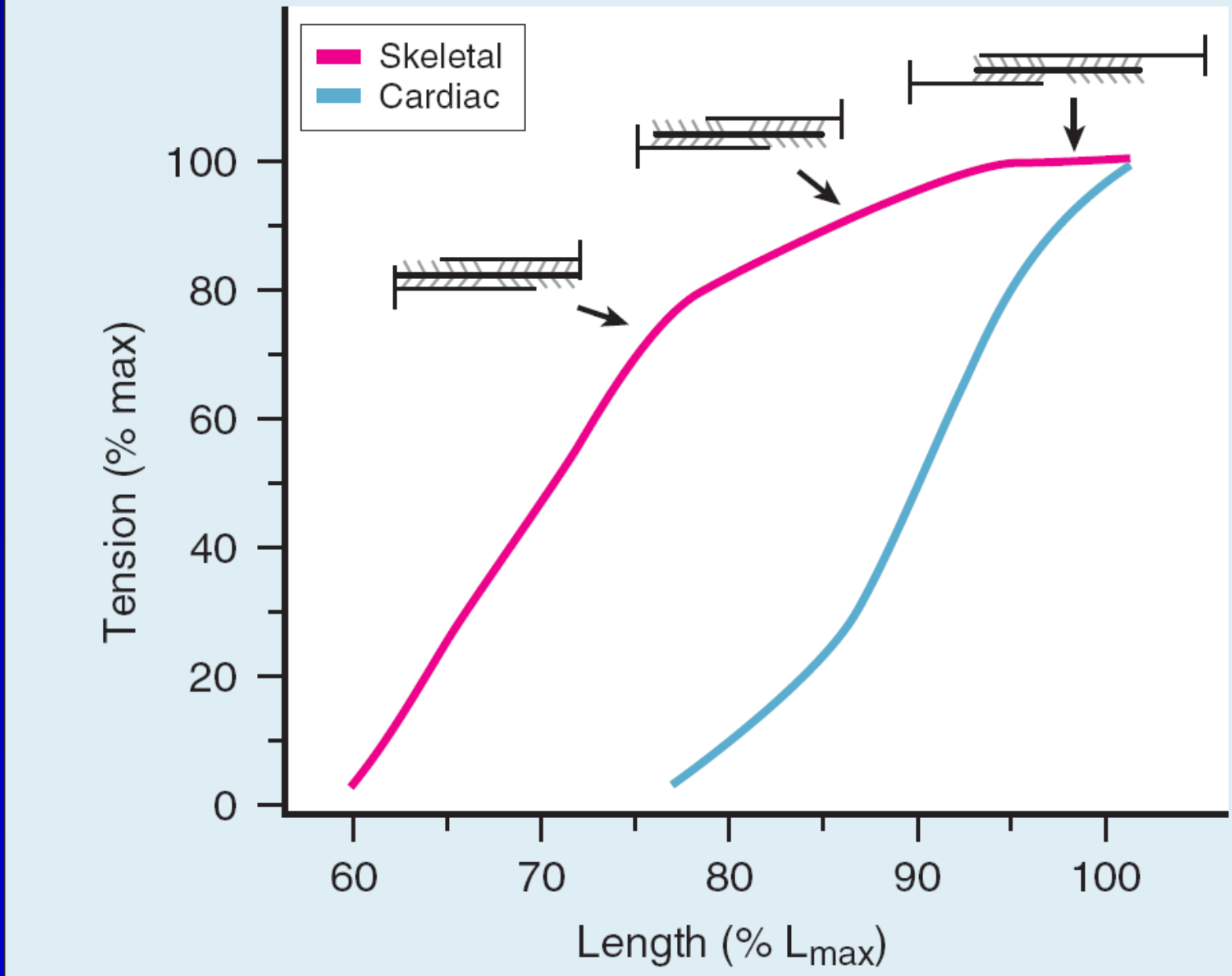

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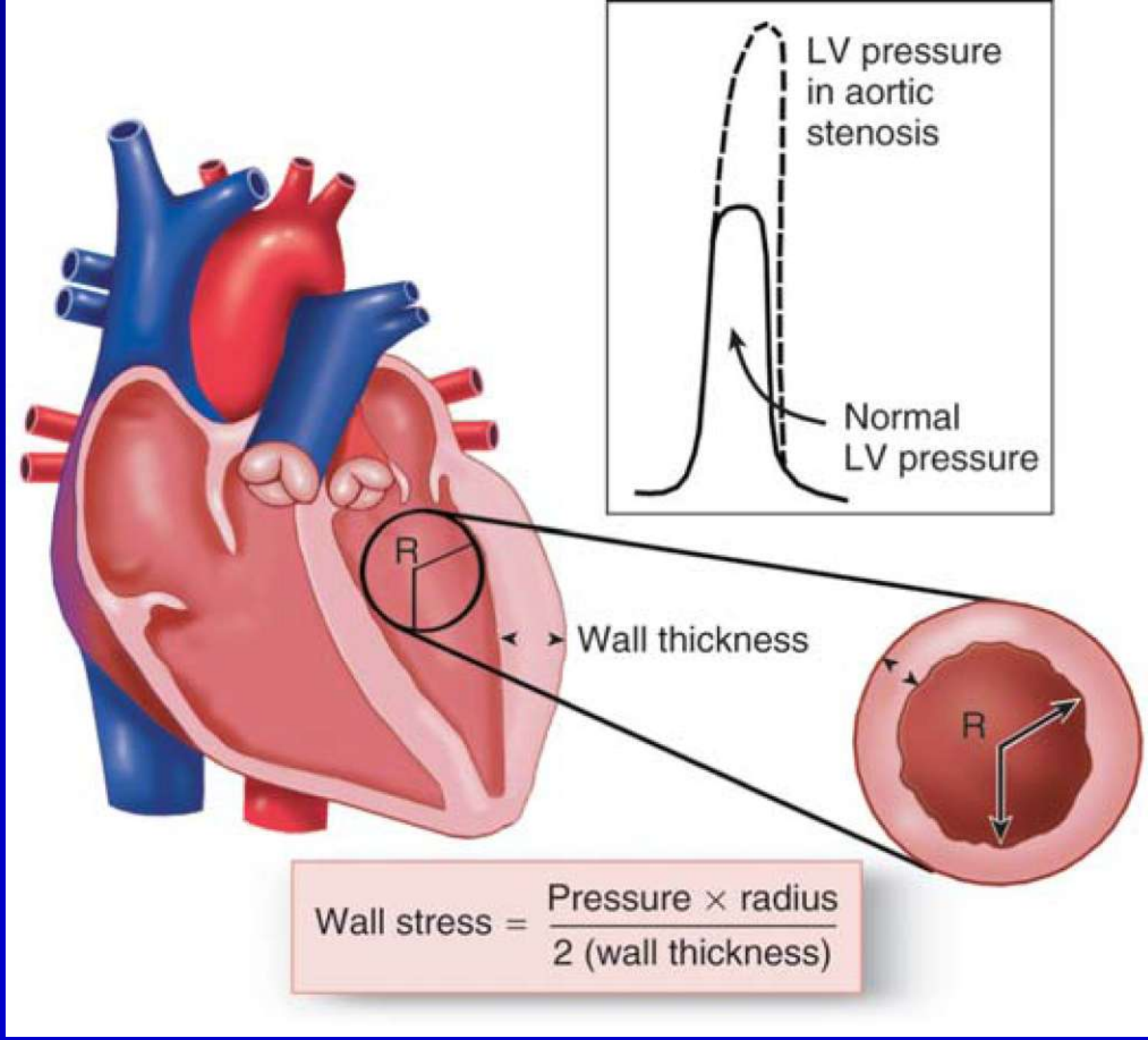

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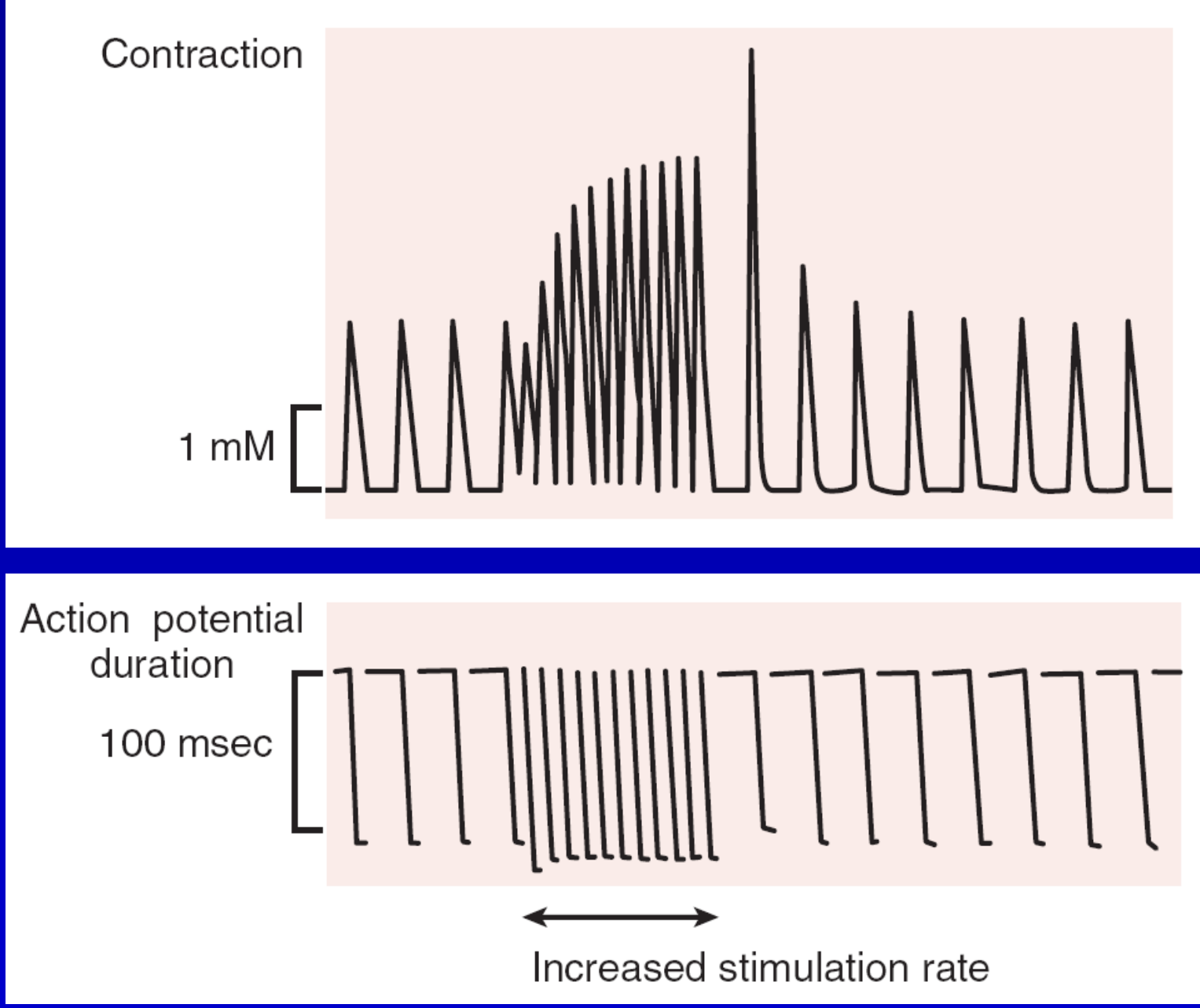

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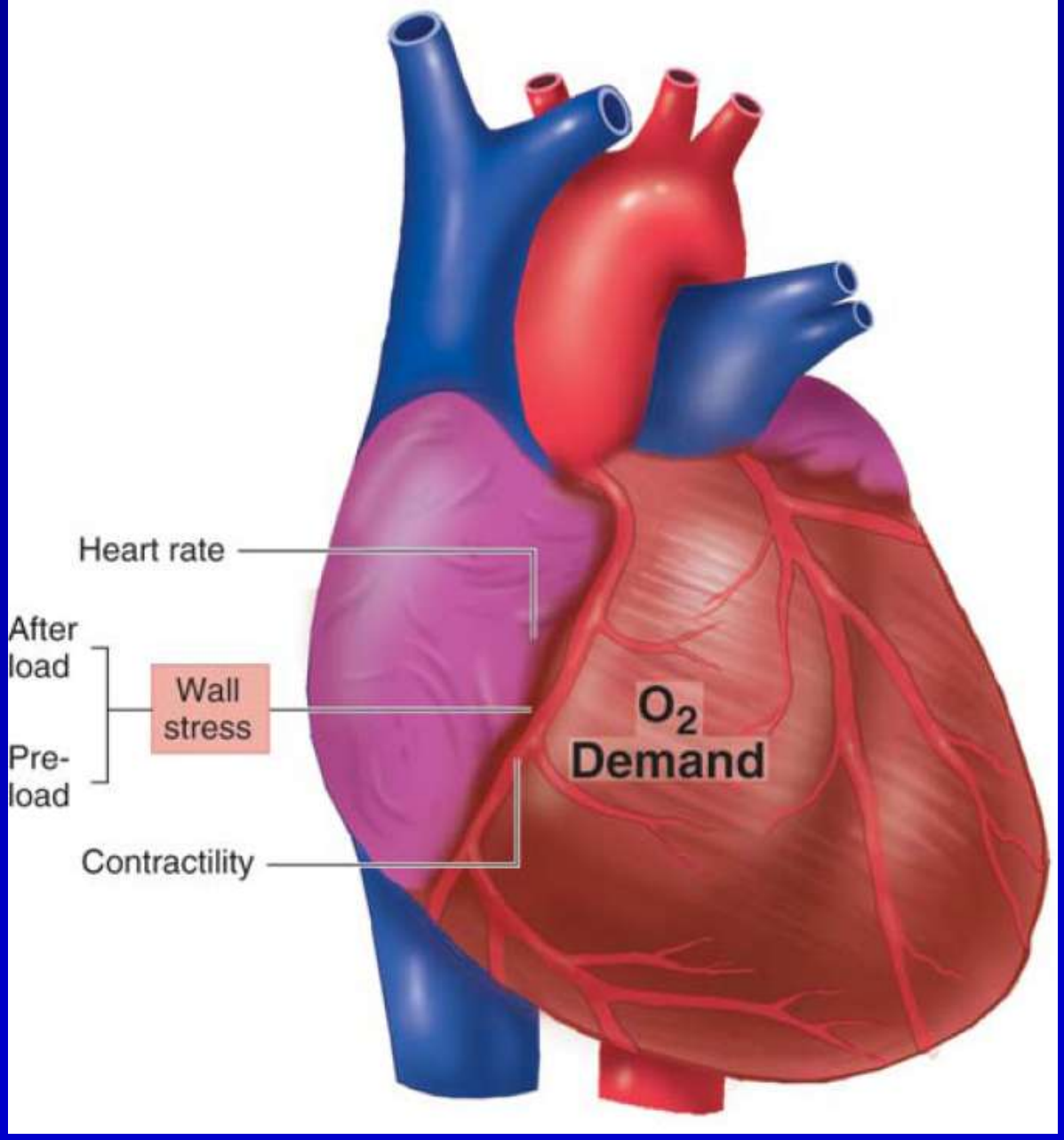

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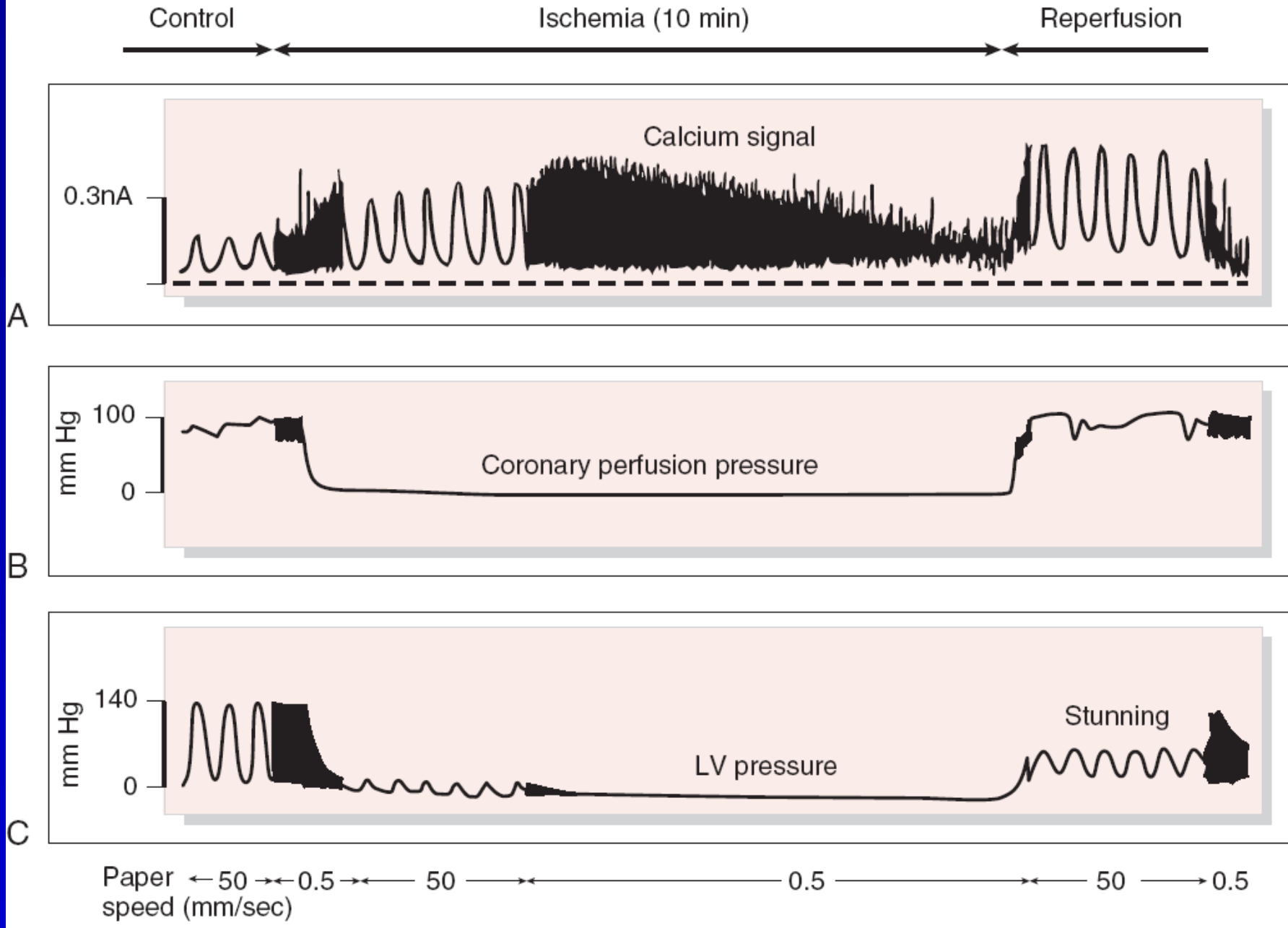

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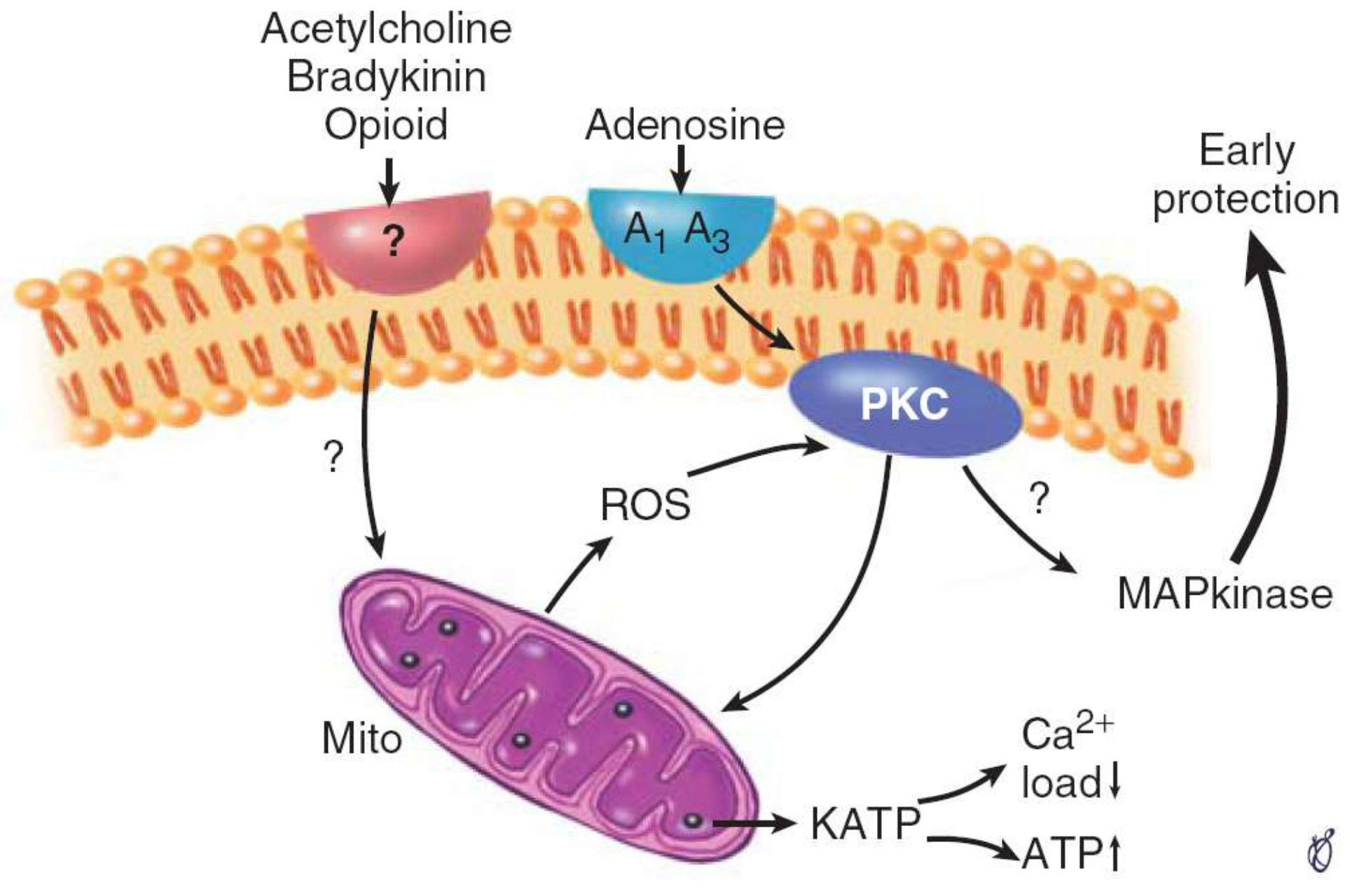

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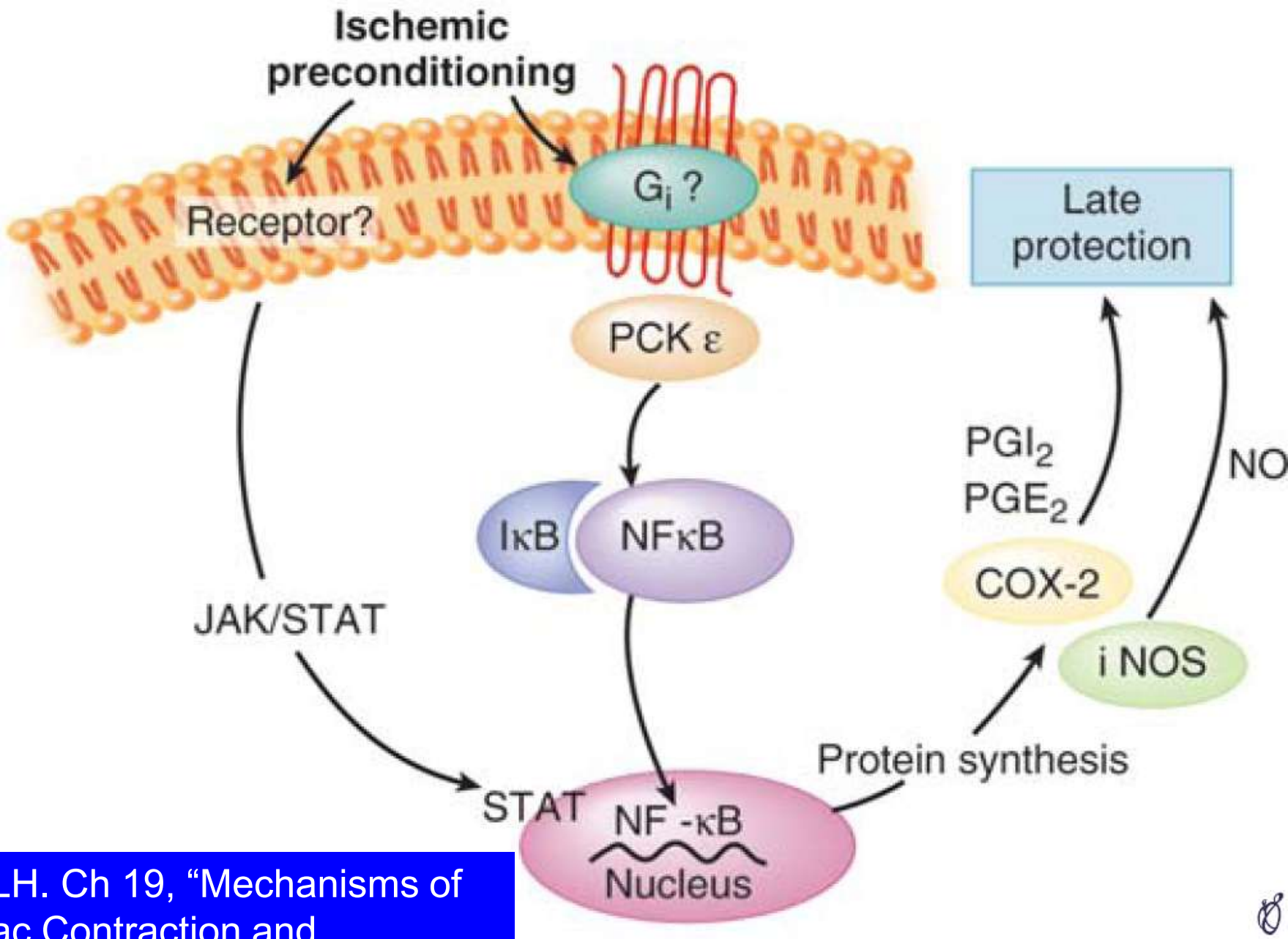

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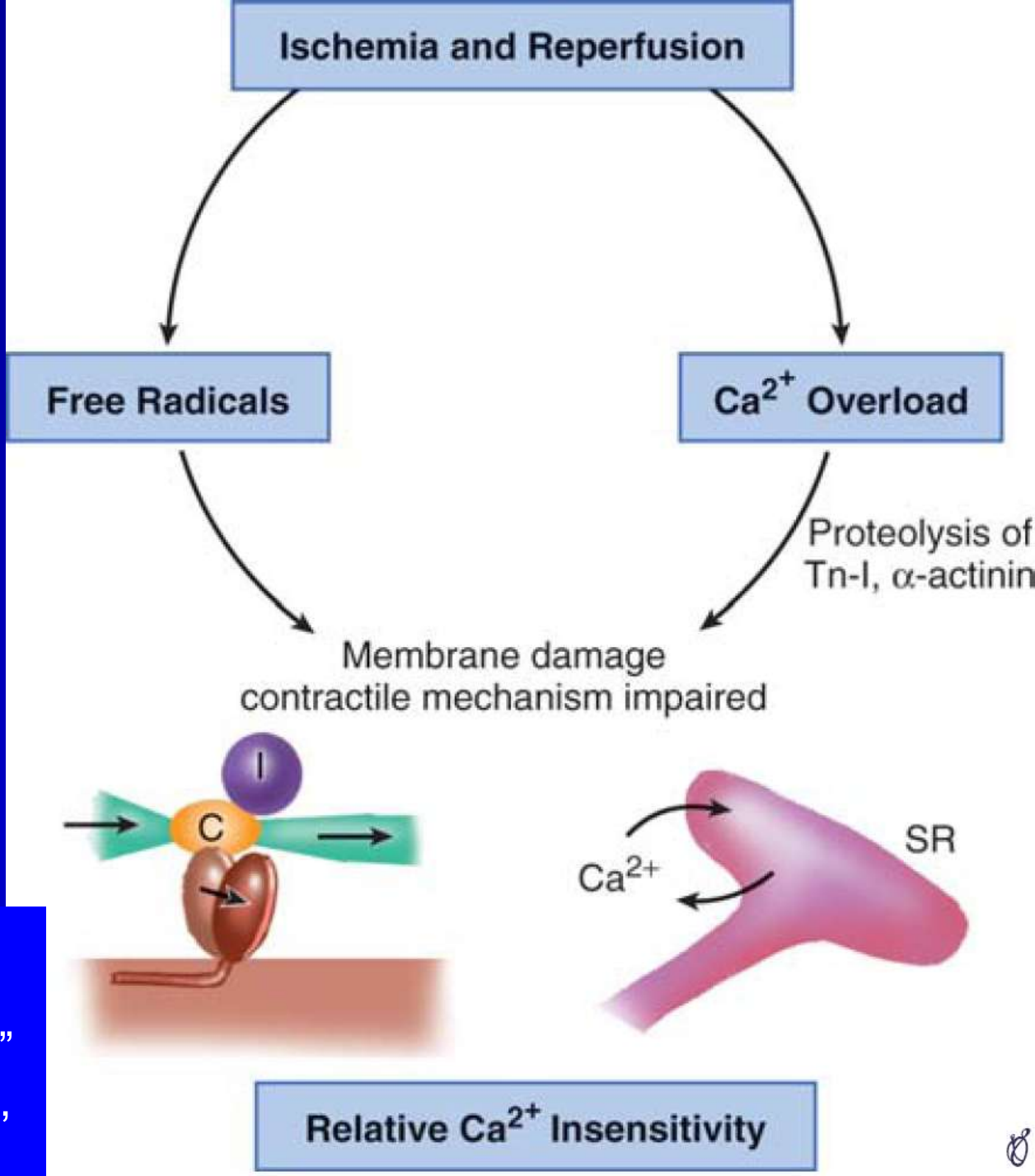

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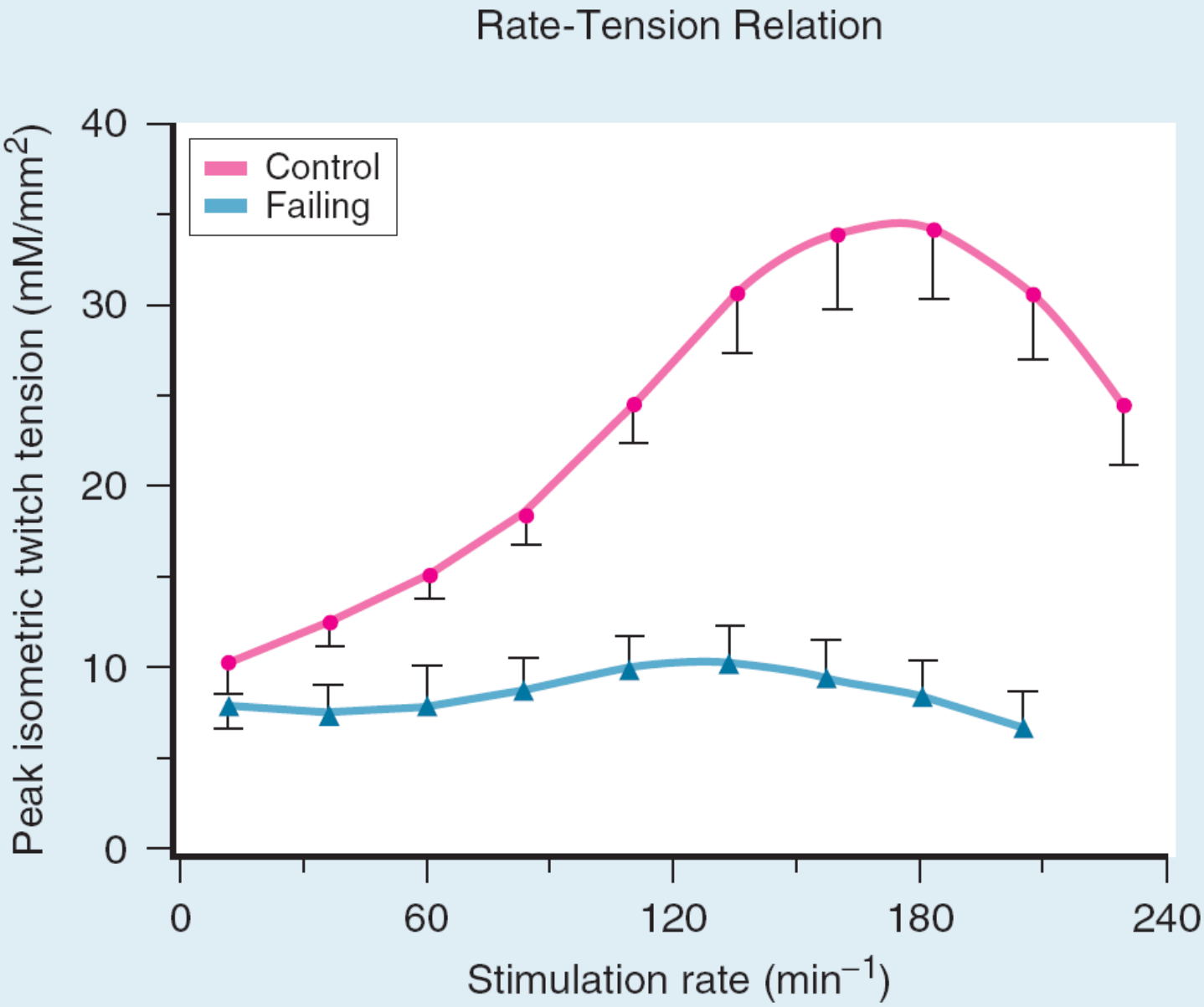

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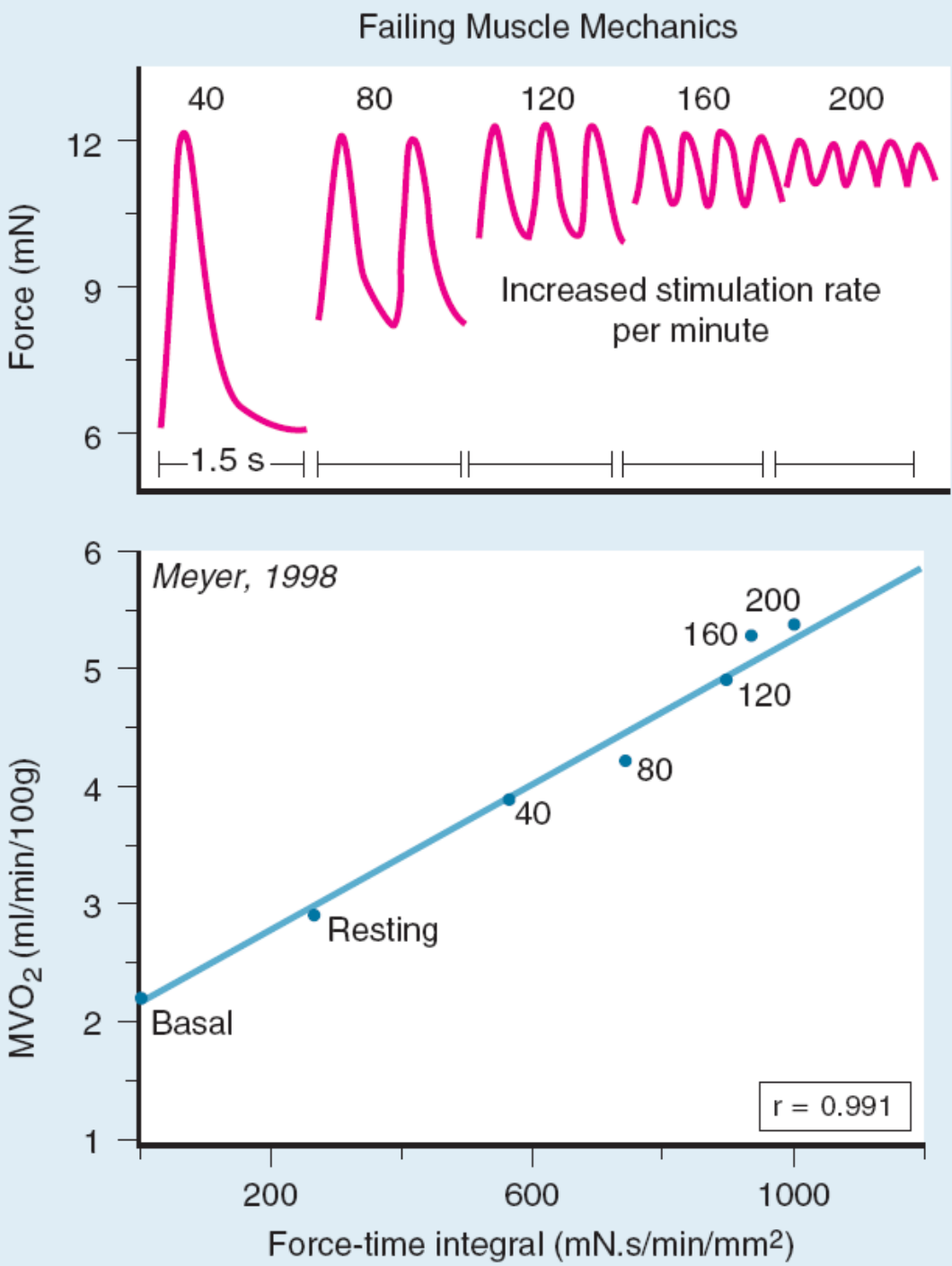

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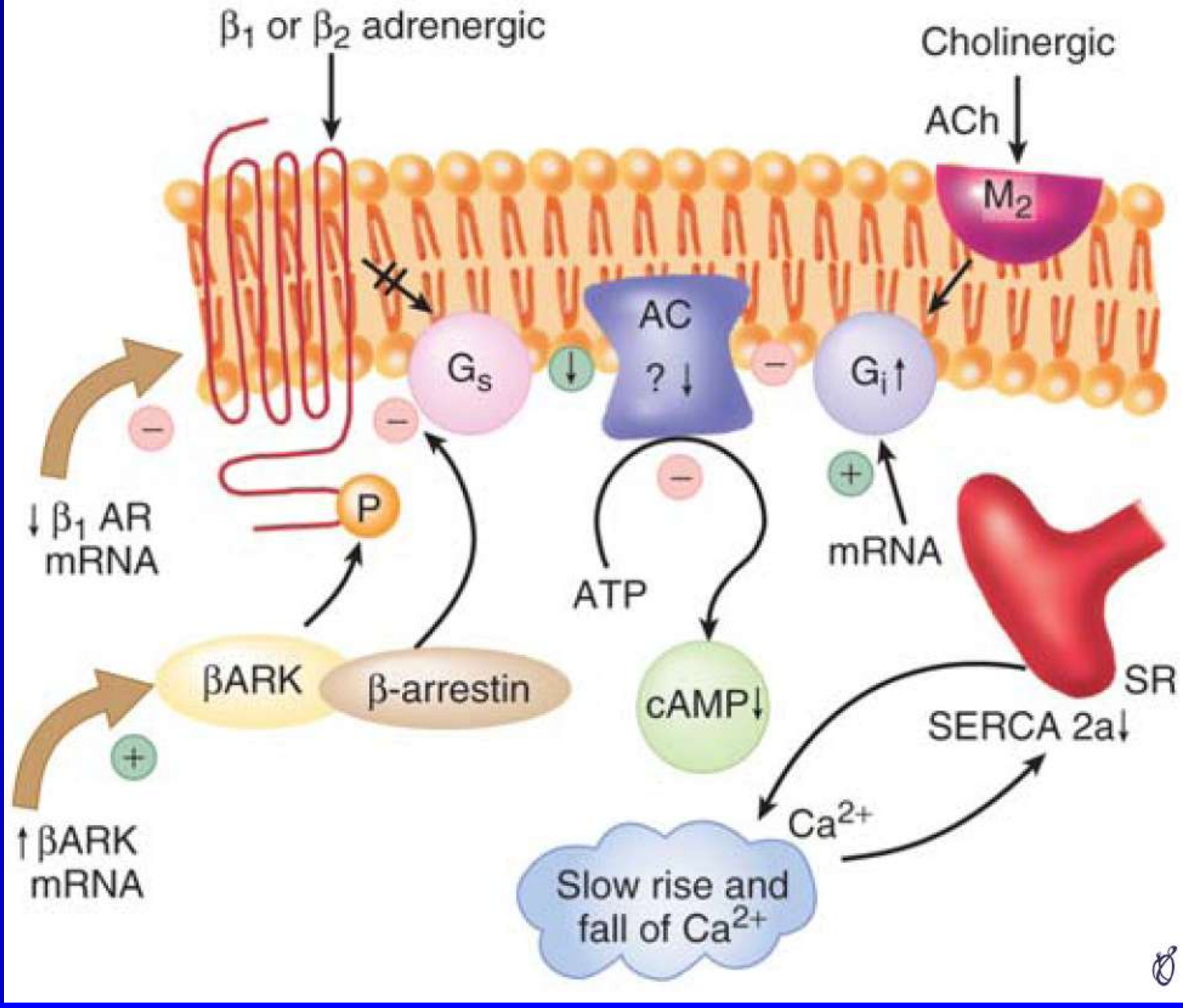

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TABLE 19–1 Characteristics of Cardiac Cells, Organelles, and Contractile Proteins

	Microanatomy of Heart Cells		
Characteristic	***Ventricular Myocyte*** [a]	***Atrial Myocyte***	***Purkinje Cells***
Shape	Long and narrow	Elliptical	Long and broad
Length, μm	60-140	About 20	150-200
Diameter, μm	About 20	5-6	35-40
Volume, μm^3	15,000-45,000	About 500	135,000-250,000
T-tubules	Plentiful	Rare or none	Absent
Intercalated disc	Prominent end-to-end transmission	Side-to-side as well as end-to-end transmission	Very prominent abundant gap junctions. Fast; end-to-end transmission
General appearance	Mitochondria and sarcomeres very abundant. Rectangular branching bundles with little interstitial collagen	Bundles of atrial tissue separated by wide areas of collagen	Fewer sarcomeres, paler
Composition and Function of Ventricular Cell			
Organelle	***% of Cell Volume***	***Function***	
Myofibril	About 50-60	Interaction of thick and thin filaments during contraction cycle	
Mitochondria	16 in neonate 33 in adult rat 23 in adult human	Provide adenosine triphosphate chiefly for contraction	
T system	About 1	Transmission of electrical signal from sarcolemma to cell interior	
Sarcoplasmic reticulum (SR)	33 in neonate 2 in adult	Takes up and releases Ca^{2+} during contraction cycle	
Terminal cisternae of SR	0.33 in adult	Site of calcium storage and release	
Rest of network of SR	Rest of volume	Site of calcium uptake en route to cisternae	
Sarcolemma	Very low	Control of ionic gradients; channels for ions (action potential); maintenance of cell integrity; receptors for drugs and hormones	
Nucleus	About 5	Protein synthesis	
Lysosomes	Very low	Intracellular digestion and proteolysis	
Sarcoplasm (= cytoplasm) (+ nuclei + other structures)	About 12 in adult rat 18 in humans	Provides cytosol in which rise and fall of ionized calcium occur; contains other ions and small molecules	

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TABLE 19–2 Ionic Effects of Adrenergic and Cholinergic Stimulation: Relation to Heart Rate and Contractile Activity

Agonist	Ionic Current	Effect
Beta-adrenergic stimulation*,†	I_{Ca} increased	+Inotropic
	I_K increased	↓APD, ↑filling time
	I_{Ks} increased‡	↓APD, ↑filling time
	I_{to} increased	↓APD, ↑filling time
	I_f increased	↑Heart rate
	I_{Na} increased	↑Contraction, ↑conduction
Acetylcholine (ACh) during beta stimulation*,§	I_{Ca} decreased	–Inotropic
	I_{Na} decreased	–Dromotropic
	I_f decreased	–Chronotropic
ACh direct effect on K^+ currents‖	I_{kACh} and I_{kATP} increased	Heart rate↓
Alpha-adrenergic stimulation¶	I_{to} decreased	+Inotropic
	I_k decreased	+Inotropic
	I_{kACh} decreased	Atrial current, effects not clear

*Data from Matsuda et al.[130]
†Data from Matsuda et al.[131]
‡Data from Volders et al.[135]
§Data from Chang and Cohen[132]
‖Data from Kurachi.[133]
¶Data from Fedida.[134]
– = negative; + = positive; ↑ = increased; ↓ = decreased; APD = action potential duration; ATP = adenosine triphosphate.

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TABLE 19–3 The Cardiac Cycle

Left Ventricular Contraction
Isovolumic contraction (b)
Maximal ejection (c)
Left Ventricular Relaxation
Start of relaxation and reduced ejection (d)
Isovolumic relaxation (e)
LV filling: rapid phase (f)
Slow LV filling (diastasis) (g)
Atrial systole or booster (a)

The letters a to g refer to the phases of the cardiac cycle shown in Wiggers' diagram (Fig. 19–19). These letters are arbitrarily allocated so that atrial systole (a) coincides with the A wave and (c) with the C wave of the jugular venous pressure.

LV = left ventricular.

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TABLE 19–4 Physiological Versus Cardiologic Systole and Diastole

Physiological Systole	Cardiologic Systole
Isovolumic contraction	From M_1 to A_2, including:
Maximal ejection	Major part of isovolumic contraction*
	Maximal ejection
	Reduced ejection
Physiological Diastole	**Cardiologic Diastole**
Reduced ejection	A_2-M_1 interval (filling phases included)
Isovolumic relaxation	
Filling phases	

*Note that M_1 occurs with a definite albeit short delay after the start of LV contraction.

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TABLE 19–6 Characteristics of Stunning, Hibernation, and Ischemia

Parameter	Stunning	Hibernation	True Ischemia
Myocardial mechanical function	Reduced	Reduced	Reduced
Coronary blood flow	Postischemic: normal/high	Modestly reduced or low normal; reduced coronary vascular reserve	Most severely reduced
Myocardial energy metabolism	Harmful effects of fatty acid fuels versus glucose	Reduced or low normal; in steady state with intermittent ischemia-reperfusion	Reduced; increasingly severe as ischemia proceeds
Duration	Hours to days; merges with delayed recovery from ischemia over weeks	Days to hours to months; occasionally longer	Minutes to hours; then lethal
Outcome	Full spontaneous recovery	Variable recovery if revascularized	Myocyte necrosis if severe ischemia persists
Proposed change in metabolic regulation of calcium	Cytosolic overload of calcium in early reperfusion with damage to contractile proteins	Hypothetically enough glycolytic ATP to prevent contracture (glucose mismatch)	Insufficient glycolytic ATP to prevent calcium overload and irreversibility

ATP = adenosine triphosphate.

Modified from Opie L, Heusch G: Lack of blood flow: Ischemia and angina. *In* Opie LH (ed): Heart Physiology, from Cell to Circulation. 4th ed. Philadelphia, Lippincott Williams & Wilkins, 2004, pp 525-552.

TABLE 19–7 Abnormalities of Calcium Cycling in Heart Failure

Subcellular	Organelle	Whole Heart	Reference
SERCA2a↓	SR Ca depleted	Negative FFR	127
RyR hyperphosphorylated	SR Ca release↓ Diastolic leak	Rate of contraction↓ Diastolic tension↑	126 136
Na/Ca exchange ↑	Released Ca extruded	Negative FFR	137
Prolonged APD and RyR changes	Cytosolic Ca↑	Diastolic tension↑ with pacing	138

APD = action potential duration; FFR = force-frequency relationship; RyR = ryanodine receptor; SERCA = sarcoendoplasmic reticulum Ca^{2+}-adenosine triphosphatase; SR = sarcoplasmic reticulum.

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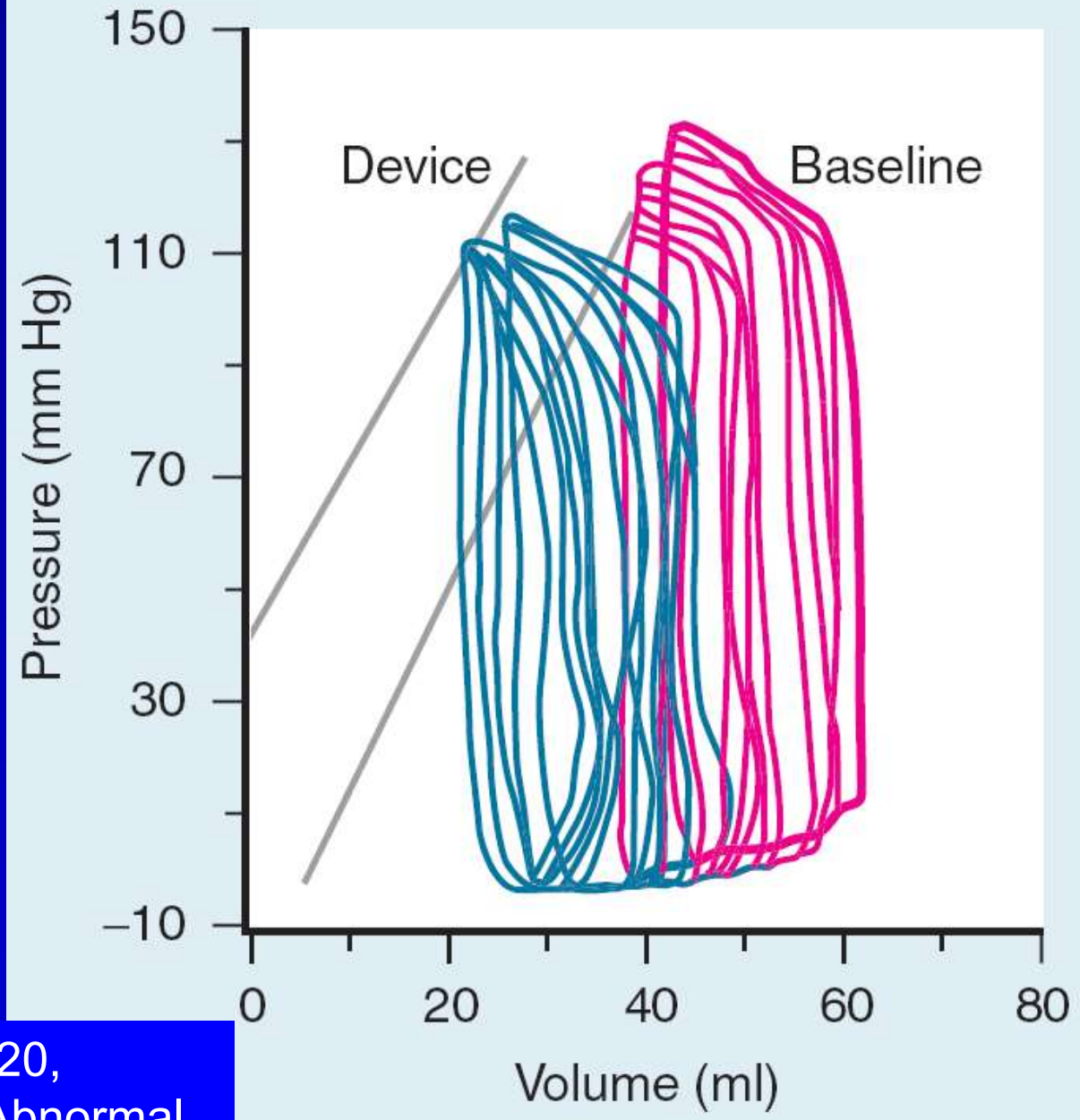

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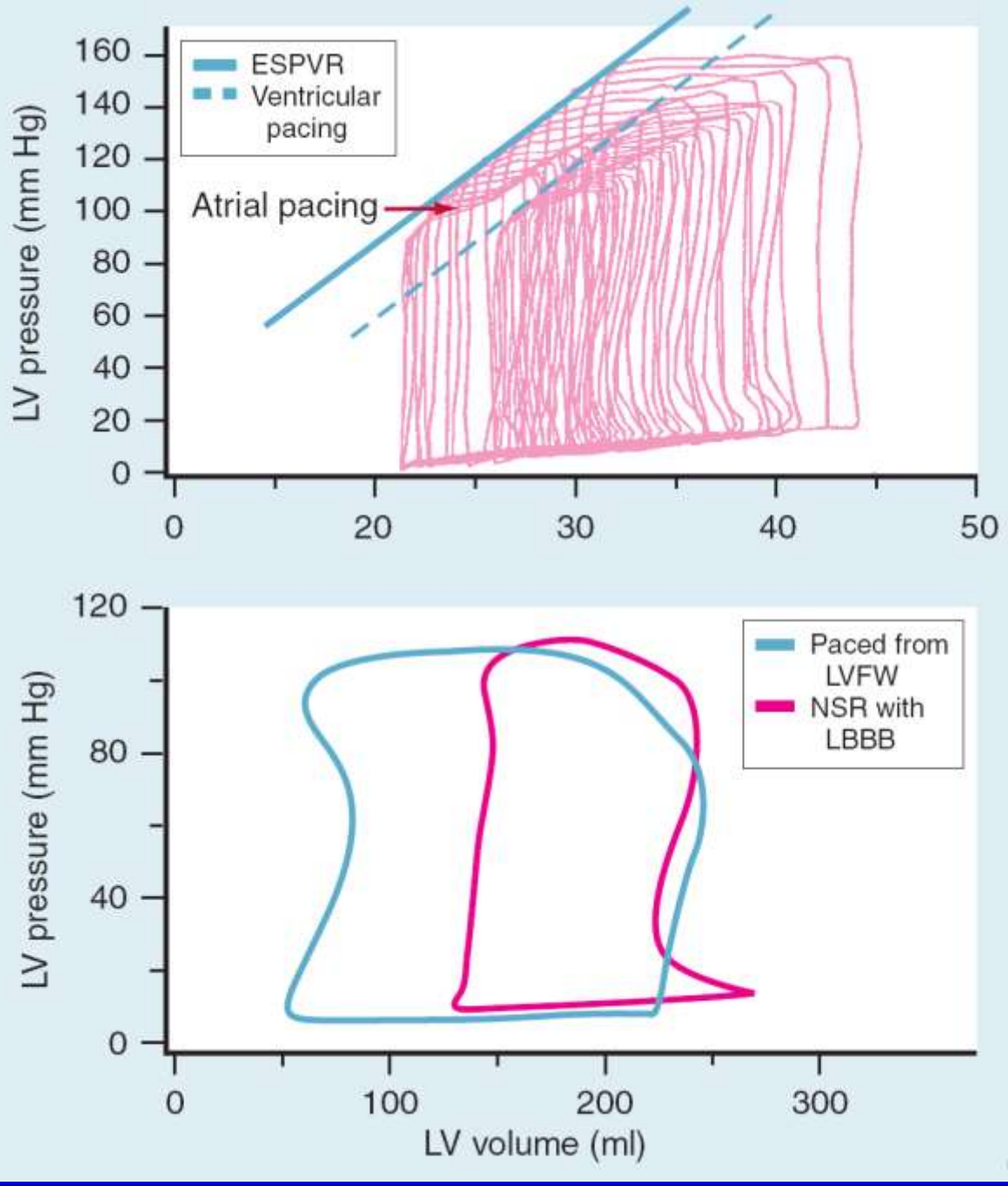

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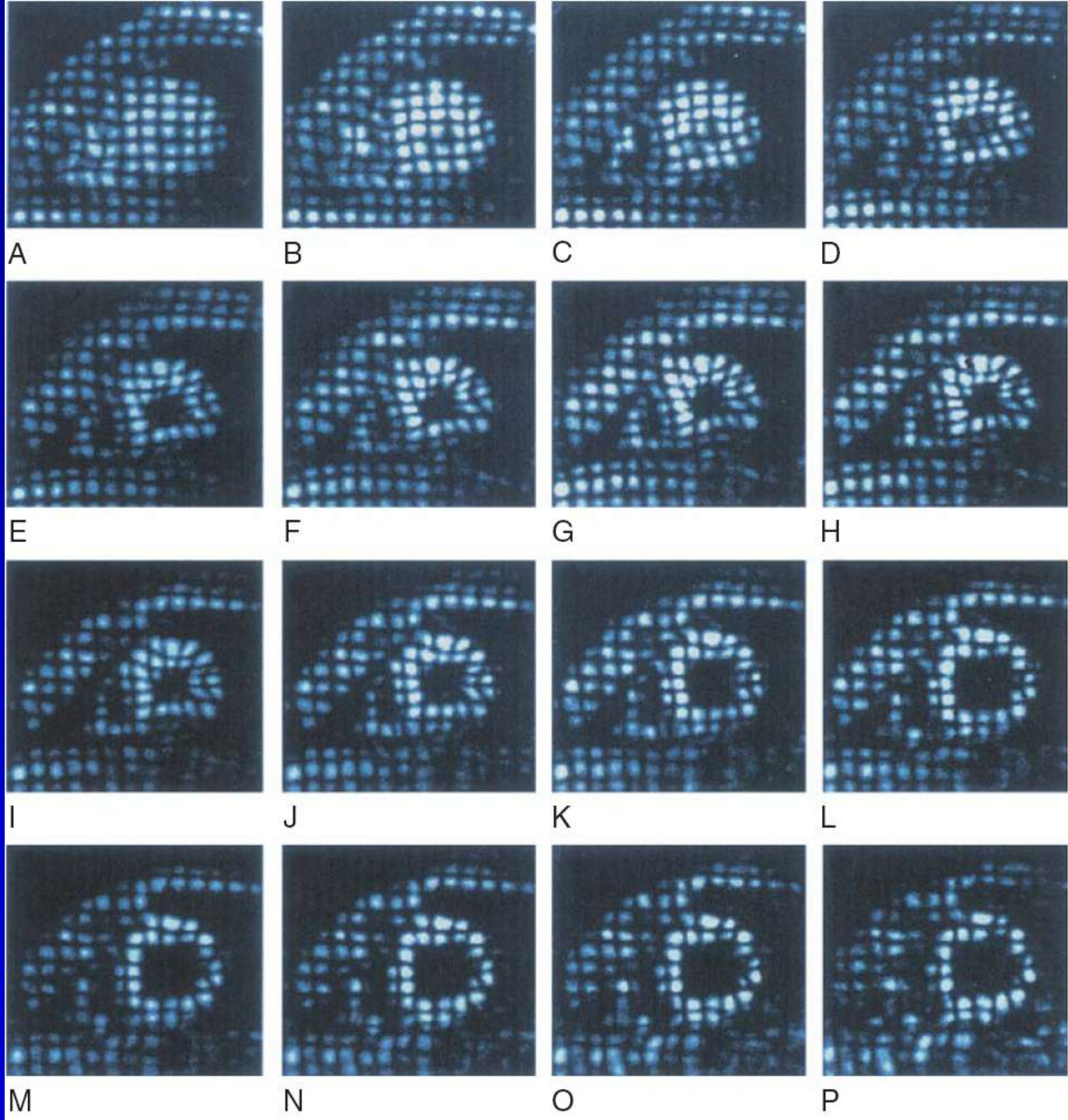

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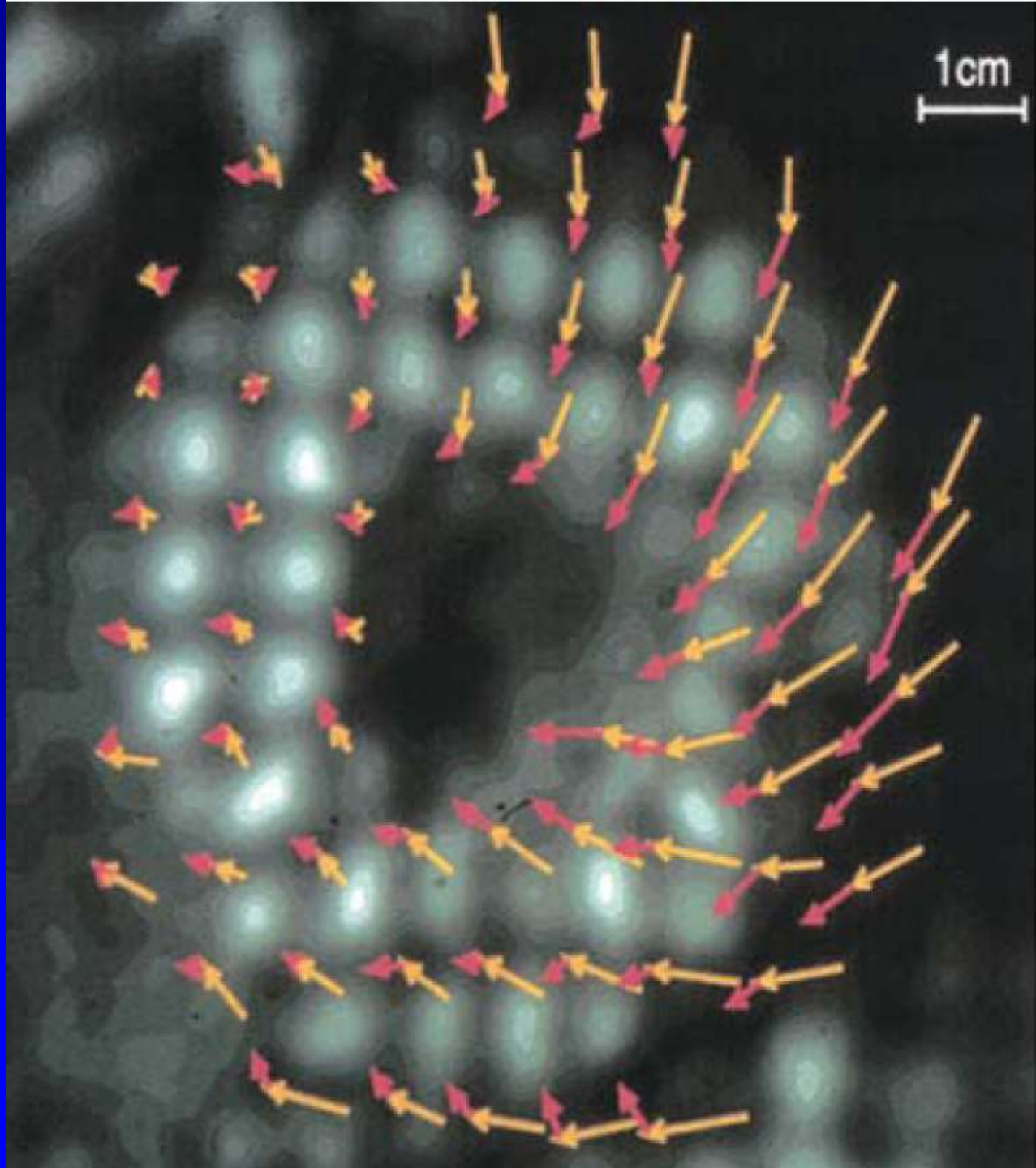

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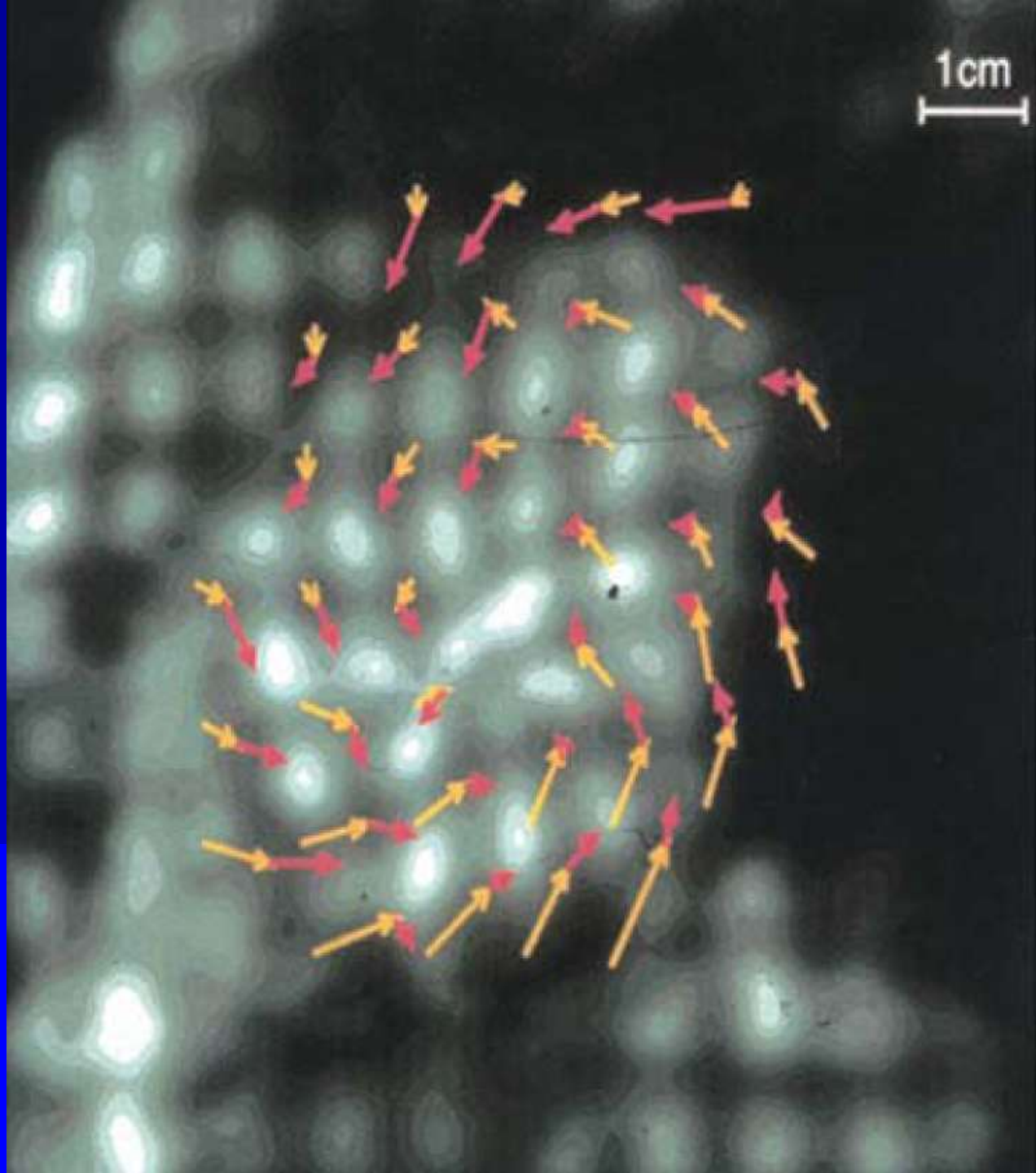

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TABLE 20–1 Uses of Cardiac Function Assessment

Diagnosis
Prognostication
Timing of intervention
Mechanism of therapy
Assessment of therapy
Detection of complications
Surrogate for clinical outcomes

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TABLE 20–2 Definitions of Terms Used to Describe Systolic and Diastolic Function

Term	Definition
Preload	Distending force of the ventricular wall, which is highest at end-diastole and is responsible for sarcomere length at the beginning of systolic contraction
Afterload	Resisting force of the ventricular wall during systolic ejection, which is necessary to overcome peripheral vascular resistance or impedance; measures of afterload are peak-systolic, mean-systolic, or end-systolic wall stress
Contractility	Intrinsic ability of the myocardium to generate force at a certain rate and time (controlled for loading conditions)
Cardiac output	Stroke volume multiplied by heart rate
Stroke work	Mean systolic blood pressure multiplied by stroke volume
Stroke force	Stroke work per ejection time
Stress	Force per area
Wall stress	Pressure multiplied by radius, divided by wall thickness × 2
Compliance or distensibility	Change in volume per change in pressure (dV/dP)
Elastance	Slope of the end-systolic pressure-volume relation
Elasticity	Property of a material to restore its initial length or geometry after distending force has been removed
Strain	Length change in percent of initial length; two definitions are used: LaGrangian strain $e = (l - l_o)l_o$ and natural strain $e = \ln(l/lo)$
Stiffness	Pressure per volume change (dP/dV). *Ventricular stiffness* is a measure for changes of the ventricle as a whole; *myocardial stiffness* is a measure for changes of the myocardium itself. Ventricular properties are characterized by instantaneous pressure-volume relations, whereas myocardial properties are best described by stress-strain relations.
Creep	Time-dependent lengthening of a material in the presence of a constant force
Stress relaxation	Time-dependent decrease of stress in the presence of a constant length
Viscoelasticity	Resistance of a material to length changes (strain) or the velocity of length changes (strain rate)

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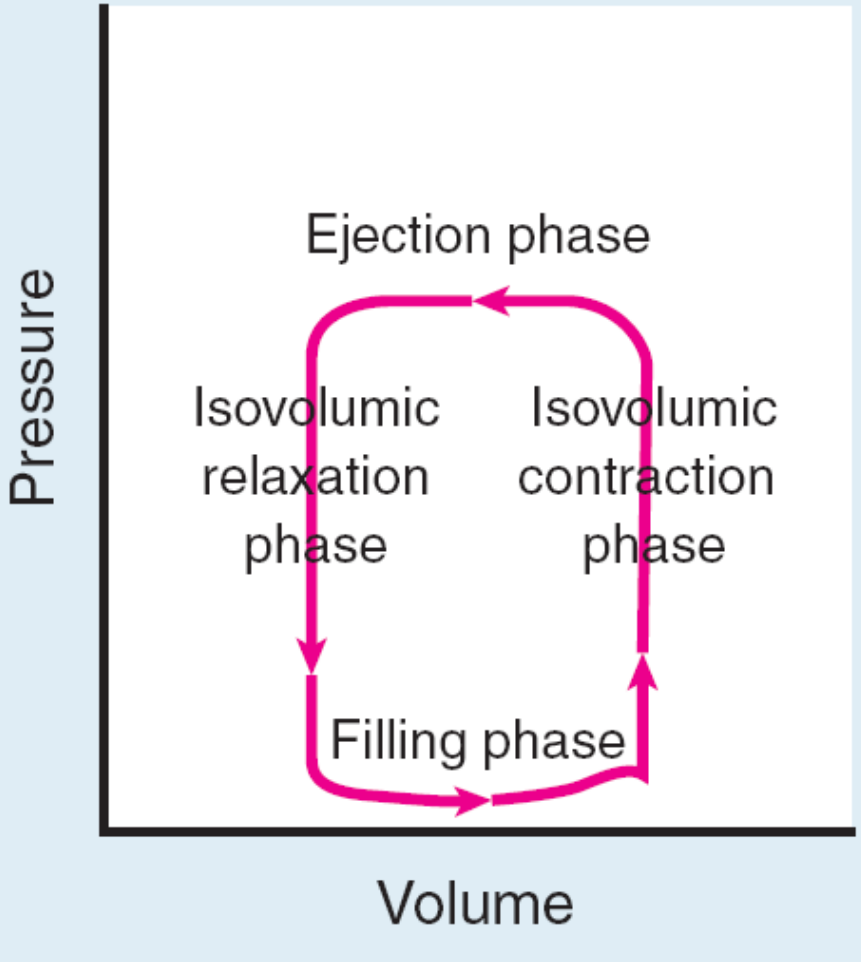

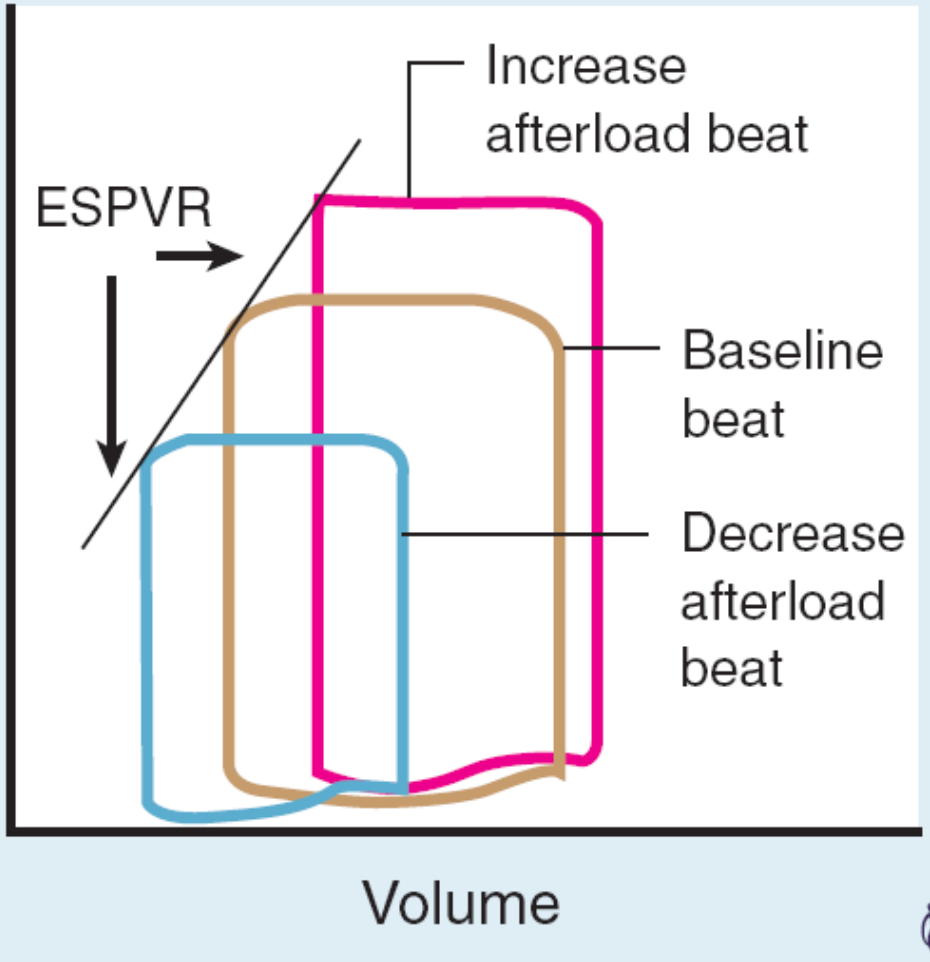

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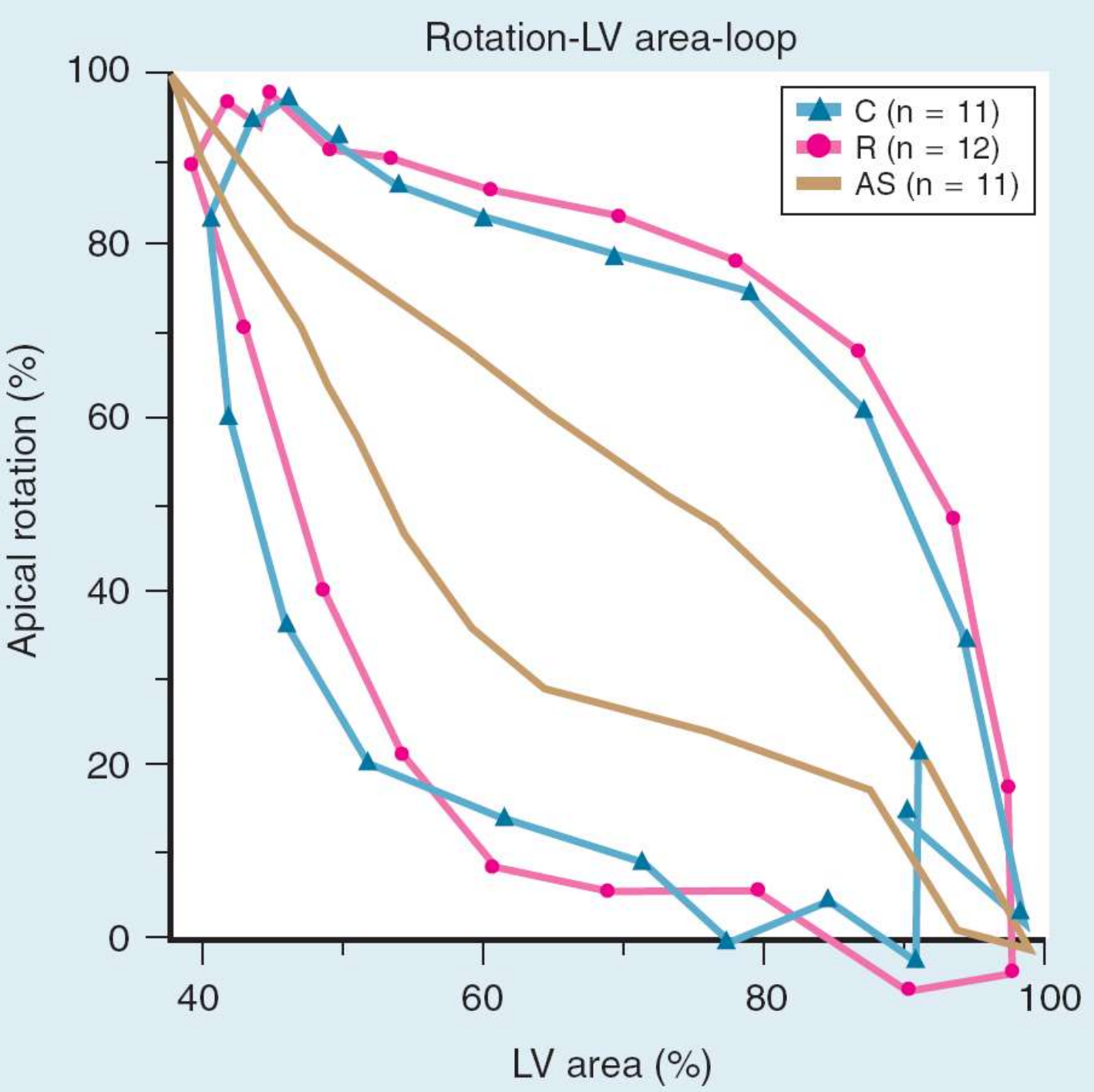

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TABLE 20–4 Characteristics of Selected Indices of Global Ventricular Function

Index	Sensitive to Inotropic Changes	Dependence On Preload	Dependence On Afterload	Dependence On Ventricular Volume or Mass	Ease of Application
Ejection fraction; fractional shortening	++	++	+++	++	++++
End-systolic volume or dimension	+	0	+++	++	++++
VCF	+++	0	+++	++	+++
Afterload-corrected VCF	+++	0	0	0	+
ESPVR	++++	0	0	+++	+
End-systolic stiffness	++++	0	0	0	+
Preload recruitable stroke work	+++	0	0	++	+
Left ventricular dP/dt	++++	++	++	++	++

ESPVR = slope of end-systolic pressure-volume relation; VCF = velocity of circumferential fiber shortening; dP/dt = rate of ventricular pressure rise.
Adapted from Carabello B: Evolution of the study of left ventricular function: Everything old is new again. Circulation 105:2701, 2002.

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–7 Echo/Doppler Assessment and MR Imaging of Right Ventricular Size, Shape, and Function

Parameter	Echo/Doppler	MR imaging
RV volume	Standard 2D views allow measurement of multiple dimensions (Fig. 20-15). The parasternal long-axis view shows the outflow tract diameter	Segmentation of individual slices provides chamber size. Adjacent areas are then summated to provide volume and shape measurements
Regional wall motion	Free RV wall and interventricular septum are imaged and paradoxical motion can easily be detected	Cine MR imaging provides contrast between the blood pool and the myocardial wall. RV wall motion is assessed using RVOT cines in the sagittal and short-axis cine images
RV mass	Approximated by wall thickness determinations along with chamber size measurements	Myocardium from the junction between the RV free wall and the interventricular septum can be traced on each slice from the base to the apex, including trabeculations. Myocardial volume computed from summated multiple slices is multiplied by 1.05 to give the mass in grams
RV wall composition	Not well studied in transthoracic images. Intracardiac ultrasound provides higher resolution data	MR imaging is potentially useful to distinguish fat from muscle
Regurgitant fraction	Doppler profiles provide semiquantitative approach	True regurgitant volumes can be measured from phase velocity maps in the main pulmonary artery and aortic root

RV = right ventricular; RVOT = RV outflow tract; 2D = two-dimensional.

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